

**AGE CHANGES IN HUMAN SKIN FROM 3 YEARS TO 75
YEARS OF AGE**



**Dissertation submitted in
Partial fulfillment of the regulations required for the award of
M.D. DEGREE
In
ANATOMY – BRANCH V**



**THE TAMILNADU
DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI
APRIL 2015**

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**THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSTY
CHENNAI, INDIA**

APRIL 2015



PSG Institute of Medical Sciences & Research

Institutional Human Ethics Committee

POST BOX NO. 1674, PEELAMEDU, COIMBATORE 641 004, TAMIL NADU, INDIA
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January 31, 2013

To
Dr S Manimegalai
Postgraduate
Department of Anatomy
PSG IMS & R
Coimbatore

Ref.: Proposal titled: '*Age changes in human skin from 3 years to 75 years of age*'

Sub.: Ethics Committee Approval for the study

The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore -4, has reviewed your proposal on 31st December, 2012 in its full board review meeting held at College Council Room, PSG IMS&R, between 2.30 pm and 4.30 pm, and discussed your application to conduct the study entitled:

"Age changes in human skin from 3 years to 75 years of age"

The following documents were received for review:

1. Duly filled application form
2. Proposal
3. Informed Consent forms in English and Tamil
4. Parental Consent form in English and Tamil
5. Assent form in English and Tamil
6. Proforma
7. Permission letter from head of the Institution
8. CV
9. Budget

The members who attended the meeting at which your study proposal was discussed are as follows:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
2	Mrs. R. Geetha	+ 2	Lay person	Female	No	Yes
3	Mr Gowpathy Velappan	BA., BL	Legal Advisor	Male	No	Yes
4	Mrs G Malarvizhi	M Sc	Nursing	Female	Yes	No
5	Mr. R. Nandakumar (Vice-Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
6	Dr. G. Rajendiran	DM	Clinician (Cardiology)	Male	Yes	No
7	Dr. V. Ramamurthy	Ph D	Biotechnology	Male	Yes	Yes



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8	Dr. M. Ramanathan	M Pharm, Ph D	Non-Medical (Pharmacy)	Male	Yes	No
9	Dr. P. Sathyan (Chairperson, IHEC)	DO, DNB	Clinician (Ophthalmology)	Male	No	No
10	Dr. Seetha Panicker	MD	Clinician (Obstetrics & Gynaecology)	Female	Yes	Yes
11	Dr. S. Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
12	Dr. Y.S. Sivan	Ph D	Social Scientist (Sociology)	Male	Yes	Yes
13	Dr. Sudha Ramalingam (Alternate Member-Secretary, IHEC)	MD	Public Health, Epidemiology, Genetics, Ethicist	Female	Yes	Yes
14	Mrs. K. Uma Maheswari	M Sc, M Phil. B Ed	Botany	Female	No	Yes
15	Dr. D. Vijaya	M Sc, Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

After due consideration, the committee has decided to approve the above proposal.

The approval is valid for one year.

We request you to intimate the date of initiation of the study to IHEC, PSG IMS&R and also, after completion of the project, please submit completion report to IHEC.

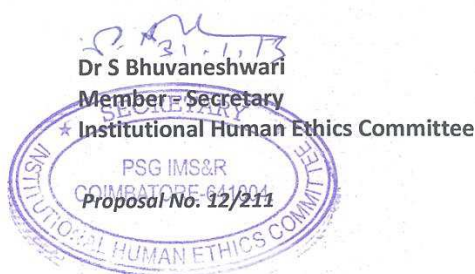
We hereby confirm that neither you nor any of your study team members have participated in the voting/ decision making procedure of the committee. The members of the committee who have participated in the voting/ decision making procedure of the committee do not have any conflict of interest in the referenced study.

This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.

PIs are required to send progress reports (in the form of an extended abstract with publications if any) to the IHEC every six months (and a month before expiry of approval date, if renewal of approval is being sought).

Request for renewal must be made at least a month ahead of the expiry of validity along with a copy of the progress report.




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CERTIFICATE

This is to certify that the dissertation title, “**Age changes in human skin from 3 years to 75 years of age**” is an original work done by Dr.S.Manimegalai, PG student, PSG Institution of Medical sciences and Research, Coimbatore, under my supervision and guidance.

Dr.S.Ramalingam, M.D

Dr.M. Jamuna M.S

Principal

Professor and HOD

PSG IMS & R

Department of Anatomy

Coimbatore.

PSG IMS & R

Coimbatore.

Place: Coimbatore

Date:

DECLARATION

I solemnly declare that this dissertation, “**Age changes in human skin from 3 years to 75 years of age**” was written by me in the Department of Anatomy, PSG Institution of Medical sciences & Research, Coimbatore, under the guidance of Dr.M.Jamuna, M.S., Professor and Head of the Department, PSG Institute of Medical sciences & Research, Coimbatore.

This dissertation is submitted to The Tamil Nadu Dr.M.G.R.Medical University, Chennai in partial fulfillment of the University regulations for the award of degree of M.D.Anatomy – Branch V examinations to be held in April 2015.

Place: Coimbatore

Dr.S.Manimegalai

Date:

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Dr.S.MANIMEGALAI

PG STUDENT

DEPARTMENT OF ANATOMY

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ABSTRACT:

Natural aging process is reflected by gradual changes in the structure of the skin. These changes become very marked in old age. The changes in the epidermis and dermis as age advances is reflected externally as wrinkling, dryness, loss of elasticity, thinning and tendency towards purpura on minor injury. So the study is done in skin specimens by grouping the individuals in 4 age groups namely Group A (3-20yrs), Group B (21-50yrs), Group C (51-65yrs) and Group D (>65yrs). The specimens were stained with Haematoxylin and Eosin stain and the changes in the thickness of the epidermis, number of Rete Pegs and the Dermo-Epidermal junction were observed. The changes in the skin appendages namely the sweat glands and the sebaceous glands were also noted. Verhoeff Van Geison Stain was done and the changes in the density and thickness of the elastic fibers and collagen fibers were noted. As the average life expectancy is increasing, the aging of skin presents a growing problem for the dermatologists. Human aging is characterized by a number of disorders like Epidermolysis bullosa and Pemphigous Vulgaris affecting the structure of the skin. So it is necessary to study the normal changes that occur in the skin as age advances which predisposes to various disorders. The study will be done among Indian population.

KEY WORDS:

Epidermis, Rete Pegs, Dermo-Epidermal junction, Dermis, Skin appendages.

INTRODUCTION

Skin is a complex organ forming 8% of the total body mass, which interacts with the environment and also protects the host from the external environment. It acts as an effective barrier against microbial invasion and maintains body temperature. It is a major sensory organ reflecting the earliest signs of various systemic disorders. It undergoes series of changes as age advances which can be studied microscopically in the various layers of the skin. These changes are reflected externally as wrinkling, dryness, loss of elasticity and various changes.

Skin has mainly two layers called epidermis and dermis. The layers of epidermis from deep to superficial are as follows. The Basal layer (Stratum basale), spinous or prickle cell layer (Stratum spinosum), Granular layer (Stratum granulosum, Clear cell layer (Stratum lucidum) and cornified layer (Stratum corneum). The first three layers are metabolically active and the superficial layers undergo terminal keratinization and cornification. Dermis has a papillary layer and a

reticular layer. The skin appendages namely the pilosebaceous units, sweat glands, sebaceous glands and hair follicles also undergo changes with increasing age.

In epidermis, the deep layer, the Stratum basale constitutes a single layer of columnar to cuboidal cells resting on the basement membrane. Cells are attached to each other by desmosomes and to the basement membrane by hemidesmosomes. These are the stem cells having increased mitotic activity, replacing the cells in the superficial layer.

Stratum spinosum, the second layer forms second layer of keratinocytes. During routine Haematoxylin and Eosin preparations, the cells shrink and detach from each other except at the sites of attachments of desmosomes, which appears like spines. The synthesis of keratin filaments is continued in this layer and they are arranged in bundles of tonofilaments. Stratum granulosum, the third layer has cells containing dense keratohyaline granules, so called the granular layer. These granules produce soft keratin of the skin. This layer also contains membrane bound lamellar granules. These granules are discharged into the intercellular

spaces in the Stratum granulosum and to the adjacent layer, Stratum lucidum if present or to the Stratum corneum. The lipid layer of the membrane seals the skin by making it impermeable to water. Stratum lucidum, the fourth layer is visible only in thick skin and is translucent. The cells are tightly packed and lack nuclei or organelles. The flattened cells contain densely packed keratin filaments.

Stratum corneum, the fifth layer has cells which are dead flattened cells filled with soft keratin filaments. The superficial cells from this layer are desquamated and replaced by new cells from the Stratum basale. The epidermis also contains melanocytes, langerhan cells and merkel cells. Melanocytes are pigment cells derived from the neural crest. The langerhan cells are antigen presenting cells. Merkel cells are mechanoreceptors for cutaneous sensations.

Dermis present below the epidermis is an irregular light staining connective tissue. The papillary layer of the dermis invaginates into the epidermis forming the dermal papillae. The deeper layer of the dermis is the reticular layer which contains dense irregular connective tissue.

Between the dermal papillae, the portion of the epidermis into the dermis is the epidermal papillae (Rete Pegs).

Skin appendages: They are the sweat glands, sebaceous glands and the terminal expanded portion of the hair follicle called the hair bulb that is present in the dermis. Attached to the hair follicles are present thin strip of smooth muscle called Arrector pili muscles found at the base of the sebaceous glands. With increasing age, epidermis and dermis undergoes atrophy. This produces changes in the external appearance, microscopic structure and also the functions of the skin. Atrophy in the epidermis is reflected as thinning, loss of basal Rete Pegs, flattening of the Dermo-Epidermal junction etc. Since there is minimal change in the thickness of the cornified layer in old age, the permeability of the skin is little affected. The rate of replacement of the cells in the superficial layer is reduced up to 50%. In the skin of elderly persons, the microscopic changes in the dermis are reflected externally as wrinkling, flaccidity, stiffness and loss of elasticity. The production of fibroblast is decreased and hence the collagen synthesis is also decreased.

With increasing age, the vascularity of the skin is reduced. The papillary loops present in the dermal papillae are affected. The cutaneous microvasculature becomes fragile which is indicated by the increasing tendency towards small spontaneous purpuric haemorrhages. The sensory receptors are decreased and so the sensitivity of the skin is affected. Since skin is the major sensory organ and it forms eight percent of the total body mass and also the microstructure of epidermis and dermis is altered and reflected externally with increasing age, it would be absolutely necessary to study the various changes that occur in the micro structure of the epidermis, dermis and the skin appendages.

AIMS AND OBJECTIVES

AIM AND OBJECTIVES

The gradual changes in the appearance and mechanical properties of the skin reflect the natural aging process. These changes become very marked in old age. The changes in the epidermis and dermis are

Decrease in the thickness of the epidermis,

Reduction in the number and the depth of the Rete Pegs,

Convuluted Dermo-Epidermal junction becomes flattened.

These changes alter the permeability barrier of the epidermis making the skin sensitive for purpurae following minor injury.

The decrease in the number of collagen fibers and elastic fibers as age advances is reflected externally as wrinkling, dryness, loss of elasticity and thinning of the skin. The orientation of the collagen fibers in the dermis is reflected as Langer's lines which is the line of approach by the surgeons. Scar formation occurs following wound healing which is due to the deposition of collagen fibers.

The elastic fibers in the dermis become more porous due to cyst and lacunae formation in old age. This increases the laxity of the skin which is reflected externally as wrinkles.

In old age the epidermis is found to be thin affecting the hydration of the skin, giving the skin a dry and cracked appearance. This makes the skin fissured and pruritic leading to a condition called xerosis. The young skin is also thin, but the hyaluronic acid is found in the dermis where the elastic and collagen fibers intersect. This hyaluronic acid is said to disappear in old skin leading to reduced hydration producing wrinkles and decreased turbidity externally. As the epidermis and dermis atrophies in old age, the skin becomes more fragile and the immune function is affected.

So a study of the changes related to the age in the layers of the skin namely the epidermis and dermis and changes in the structure of the skin appendages namely the sweat glands and sebaceous glands is done.

As the average life expectancy is increasing, the aging of skin presents a growing problem for the dermatologists. Human aging is characterized by a number of disorders that affect all tissues. So it is necessary to study the normal changes that occur in the skin as age advances which predisposes to various disorders. The study is done among Indian population.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Graham J S et al (1965) has studied the changes in the human skin. The changes in the skin are mainly due to prolonged exposure to sun. The collagen fibers of the dermis are found to be thickened due to decrease in the neutral and acid mucopolysaccharides. Collagen forms about one-third of the total body protein, out of which half of the collagen is present in the skin. The density of collagen was found to increase in sun non-exposed areas and was also found to increase in the early ages and then was found to decrease in sun exposed areas. The collagen fibers close to the epidermis were observed to be small, but the collagen fibers present deeper were found to become larger.

The dermis and epidermis grows in opposite directions, with the dermis growing outwards and the epidermis growing inwards. So the dermis as it grows pushes the newly formed elastic fibers inwards along with it. The non fibrous proteins, acid and neutral mucopolysaccharides were found to decrease and the fibrous proteins, collagen and elastin were found to increase as age advances. In sun exposed skin, the acid and

neutral mucopolysaccharides and elastin increases and the amount of collagen decreases.

Neil A .Fenske (1986) has studied the structural and functional changes of the normal aging skin. The overall thickness of the epidermis was found to be reduced. But the thickness of the Stratum corneum was unaltered. The cells of the basal layer, the Stratum basale of aged skin showed variations in the size, shape and staining features than young skin. Above the Stratum basale, decrease in the vertical height and increase in the surface area of the keratinocytes were noted. This altered cellular morphology can be the cause for dryness of the skin in elder individuals.

The number of interdigitating papillae per unit surface area starts to get decreased in persons from 21 to 40yrs of age leading to flattening of the Dermo-Epidermal junction at 61-70yrs of age. This can be the reason for increased tendency towards shear type injuries and bullae formation in older persons. Decrease in the number of melanocytes was noticed in both sun exposed and unexposed areas from the age of 30years.

The density and cellularity of the dermis was decreased with increasing age. The amount of collagen decreases but there is thickening of the collagen fibers. The elastic fibers were loosely arranged and fragmented by 50 -70years of age. These changes are more marked in the elastic fibers of the dermis over 70years of age. The following changes in the collagen and elastic fibers of the dermis predispose the skin to injury, sagging and loss of resiliency and recoverability following stretching. The number of sweat glands was reduced. The number of sebaceous glands was not altered, but the size of the gland was found to increase in old age.

Tsuji .T (1986) has studied about the wrinkles of skin in aged persons from 67 to 82 years of age in males and females. The epidermis was found to be thin and flattened in the face and neck. The papillary dermis showed degeneration. In the area of wrinkle, the epidermis was depressed and papillary dermis showed less degeneration, whereas in abdomen the elastic fibers in the papillary dermis were found to be decreased or almost disappeared. So the changes in the elastic fibers in the dermis in old age is said to play the main role in the formation of wrinkles which is reflected externally.

Robert M. Lavker et al (1987) stated that the epidermis was thinner in older people than in younger people. Rete Pegs were found to be retracted in older skin resulting in flattening of the Dermo-Epidermal junction. This flattening can be due to the decrease in the proliferative capacity of the epidermis in aged persons. The cells in the basal layer of the epidermis showed changes in the size, shape and staining qualities. The nucleus was found to be shrunken with clumping of keratin filaments and the organelles in the cytoplasm was found to be condensed. These changes were found to produce dark staining keratinocytes, which represented the dying cells.

In the young skin the basal layer of the epidermis, the Stratum basale exhibited numerous villi like cytoplasmic projections into the epidermis giving a serrated appearance. These processes produced a convoluted appearance resulting in a convoluted Dermo-Epidermal junction in the skin of younger individuals.

The components of the Dermo-Epidermal junction were retained in the aged epidermis namely the hemidesmosomes, anchoring fibrils, and lamina densa and lamina lucida. In aged individuals, there was reduplication of the lamina densa with its associated anchoring fibrils and was found periodically below the keratinocytes and melanocytes. This

reduplication compensates for the flattening of the Dermo-Epidermal junction due to retraction of the Rete Pegs, to bind the epidermis to the underlying dermis. It has been reported that there is no alteration in the cellular layer of Stratum corneum in old age and it was found to retain its normal thickness and resistance.

The sebaceous glands were found to increase in size with increasing age. Number of melanocytes was found to decrease with increasing age. The collagen fibers of the dermis are arranged as tightly packed fibers in the young persons and loosely packed straight fibers in old individuals. This increases the tensile strength of the collagen fibers in older skin and the skin becomes less stretchable. In older skin the elastic fibers disintegrate into short fibrils.

Shuhei imayama (1989) has studied the changes in the collagen and elastic fibers using the rats from ages of 2 weeks to 24 months. Post natal growth of the collagen fibers is characterized by the arrangement of collagen fibers in straight bundles. As age advances the collagen fibers were found to become more straightened and the fibers bend and dislocate the elastic fibers. Deformation of the elastic fibers occurs in adulthood.

The elastic fibers was found to be highly tortuous and distorted around the collagen bundles in older age group. This causes the locking of two fibers, the collagen and elastic fibers together, so that the two fibers cannot function separately. This decreases the compliance of the connective tissue of the dermis causing sagging and laxity of the skin.

Catherine Escoffier (1989) has explained that there is no variation in skin thickness from 15 to 65 years of age. The skin is found to be thin before 15 years and after 65 years. The skin of 90 years age group is found to be thinner than the skin of 5 years age group. Though the epidermis plays the major role in protecting the skin from the environment, the dermis which is fibrous, made of collagen and elastic fibers is found to play the major role in protecting the skin from mechanical stresses. Due to various movements of the body the dermis is subjected internally to continuous stress which is reflected externally as Langer's lines. Numerous spaces are found to appear in between the fibrous network of the dermis in the adult skin. These spaces were found to disappear in aged skin which might be the reason for the decrease in the thickness of the epidermis after 65 years of age.

Kurban RS (1990) has observed the epidermal changes as flattening of the Dermo - Epidermal junction, decrease in the number of melanocytes and decrease in the cellularity of dermis. In the dermis, the number and the diameter of the collagen fibers was found to be attenuated in the papillary dermis and the number and thickness of the elastic fibers was found to be increased in the reticular dermis. The density of the collagen fibers was found to be increased forming a coarse network. Decrease in glandular activity with increasing age has also been noted.

Montagna W (1990) has reported that one of the common flaws in studying the age changes in human skin is the tendency to generalize the changes although some of these generalizations cannot be avoided like graying of hair at certain areas in certain persons while premature aging occurs in some persons. Sun is the major factor causing unpleasant alterations in the exposed skin. This study explains that the epidermis is little affected but the ridges on the undersurface of the epidermis are found to be flattened. The Dermo-Epidermal junction is not found to be completely flattened in old age, but the Rete Pegs were found to be blunt. The structure of the sebaceous gland is little affected but the size

increases a little larger in old age. The number of melanocytes decreases in old age.

The dermis is found to become acellular with decrease in number of fibroblasts, mast cells and macrophages, but the dermis of sun exposed skin is rich in cells. The blood vessels are found to be dilated. The elastic fibers were found to be distorted and the collagen fibers were also distorted and loosely packed in the dermis.

Faten S et al (1991) has studied the histological changes in the skin. With Haematoxylin and Eosin stain, the layers of the epidermis have been studied. He has explained about the different layers of the epidermis namely, the Stratum basale in the basal region which was found to have a single layer of columnar cells and the cells were found to have deeply staining basal nuclei and many mitotic figures. Immediately above the basal layer was found the prickle cell layer, the Stratum spinosum which was found to have number of layers of polyhedral cells and the cells were found to have a round, central nuclei with number of clear cells in between the polyhedral cells. Above this layer was found the granular layer, the Stratum granulosum which was found to contain number of

layers of flattened cells with flattened nuclei. The outermost layer was the horny layer, the Stratum corneum which was found to contain number of dead cells of acidophilic squames without nuclei. The epidermis of younger subjects was found to be thinner. The cells in the basal cell layer, the Stratum basale showed variation in the size, shape and staining characteristics. Some cells were darkly stained and other cells looked pale. The dark staining was due to condensation of cytoplasmic organelles, shrunken nucleus and the clear cells were found to be non functioning melanocytes. The decrease in the number of Rete Pegs in old age affects the proliferative activity of the epidermis. This decrease in the number and the depth of the Rete Pegs has showed flattening of Dermo-Epidermal junction in older age group. In old age the skin was found to be more susceptible for the formation of blisters externally involving the Stratum corneum internally. The reepithelialisation of the Stratum corneum is affected in old age and hence the ability to repair wounds is also affected.

The dermis has been studied with Orcein stain. Just below the Dermo- Epidermal junction, brush like pattern of fine elastic fibers has been noted. In the reticular dermis, the elastic fibers were found to form a network. These changes were noted in young skin whereas in old

individuals the elastic fibers were found to be small, fragmented and randomly distributed in older persons. The collagen fibers have been studied with Van Gieson stain which has showed fine collagenous fibers in the papillary dermis and thick coarse collagenous fibers in the reticular dermis in younger persons. Whereas in aged persons the collagen fibers were found to be decreased in papillary dermis and focal areas of depletion was noticed in the reticular dermis. With Masson trichrome stain, the papillary dermis was found to be more cellular than the reticular dermis. Fine collagenous fibers has been noticed in the papillary dermis and dense collagen fibers has been noticed in the reticular dermis in young adults and in aged individuals the collagen fibers were found to be decreased in papillary dermis and focal areas of depletion has been noticed in the reticular dermis.

Esmat Z. Gheigh (1991) has categorized the subjects into 3 group's, 20-40years, 40-60years and 60-78years of age. Group 1 showed undulating Dermo-Epidermal junctions and group 2 and 3 showed flattened Dermo-Epidermal junctions. The dermis of group 3 was found to be acellular and avascular compared to group 1 and 2. The elastic

fibers were loosely formed and showed cysts and lacunae in aged individuals.

The epidermis of group 1 and 2 has showed 2 types of keratinocytes. The first type was cuboidal in shape and was located in the deep Rete Ridges. Prominent melanosomes were found around the apical portion of the nucleus. The second type was columnar in shape located at the shallow ridges. Melanosomes was less in number and their cytoplasmic processes extended into the dermis. The above mentioned 2 types of keratinocytes were less distinct.

This study has reported that the collagen fibers were increased in the papillary and reticular dermis in persons of 20 years to 40 years of age. In aged individuals in the dermis the content of the collagen fibers were found to be decreased. The content of elastic fibers was increased, but the fibers appeared disorganized and showed areas of fragmentation and distortion. The avascularity of the papillary dermis in aged persons would be the reason for pallor of the skin. This can be the reason for hypothermia which is a problem usually encountered in aged individuals.

J.L. Contet-Audonneau et al (1999) have studied 46 subjects of both sexes between 57 and 98 years of age. They have proved the thinning of the epidermis, flattening of Dermo- Epidermal junction, disappearance of dermal papillae and distortion of elastic fibers in the epidermis with increasing age in sun protected areas. This author has reported that, chronic exposure to sun produces atrophy of all the skin layers but the elastic fibers in the dermis has been found to hypertrophy.

The desmoplakins are the kinds of proteins found at the contours of the keratinocytes. The reduction in the desmoplakins and the number of cellular layers of the epidermis was found to be the reason for the thinning of the epidermis. The decrease in collagen fibers in dermis in old age produces weakening of the Dermo-Epidermal junction leading to mechanical instability.

Zouboulis C. C et al (2001) explains that skin is the major organ reflecting the changes with increasing age. The authors have mainly concentrated in the changes in the sebaceous gland as age advances. 90% of the changes in the skin are due to chronic sun exposure. Pilosebaceous unit develop between 2-4months of gestational age.

First the hair follicles develop followed by the development of the sebaceous glands. These were well developed in neonates following which there was marked decrease in size of the glands at birth. The glands become undetectable during childhood. With the onset of puberty, the size increases reaching the maximum at third decade of life. Then the size remains constant at middle age and starts decreasing slowly at the seventh decade. So there is no change in the number of sebaceous glands with increasing age, only the size varies. In elderly adults, the activities of the sebaceous glands depend on the sex of the individual. In males until the eighth decade the size is comparable with that of the young person's only.

In females the secretion of sebum falls after menopause. Its size decreases to 40% in the sixth decade and continues to fall in the seventh decade after which there is no further reduction in size. The decrease in androgen level in old age can cause decrease in the cellular turnover of the sebaceous gland of face. Though the activity of the sebaceous gland is decreased in aged individuals, both males and females respond to androgens when given externally and the level of sebum can be increased. The effect of sunlight on this sebaceous gland was more influenced on the facial skin. This was found to be the cause of the

hyperplasia of the sebaceous glands. The clinical problem encountered in late adolescence with reduced size of the sebaceous glands is skin xerosis.

Kirsten Sauermann et al (2002) have studied the age related changes in skin and have measured the thickness of the horny layer and the size of the cells in the granular layer. The cells of the granular layer, the Stratum granulosum was found to be large with dark staining nuclei and the cytoplasm of these cells were found to contain numerous granules in a 23 year old person. The diameter of these cells was found to be bigger in older age group than younger age group. No difference was found in the thickness of the horny layer. The decrease in the overall thickness of the epidermis was noted.

The height of the Dermo-Epidermal junction was found to be decreasing with increasing age. Decrease in number of dermal papillae per area and changes in the thickness of the basal layer were found to be the reason for the flattening of the Dermo-Epidermal junction in still older individuals.

Sophie Bosset et al (2002) have done a histological analysis of the epidermis and dermis of skin. This study says that chronic exposure to sun predisposes to the formation of wrinkles with other changes like, atrophy of the epidermis, increase in the number of melanocytes, accumulation of truncated elastic fibers, decrease in the number of collagen fibers and flattening of Dermo-Epidermal junction.

Jean Kanitakis (2002) says that the skin occupies 50% of the total body weight in adult humans. Epidermis and the skin appendages develop from the ectoderm and the dermis from the mesoderm. Epidermis has a stratified epithelium with 90-95% of keratinocytes. These cells are arranged continuously in four layers with the superficial layer, the Stratum corneum forming a protective barrier of the skin. The Stratum basale has a single layer of keratinocytes, the Stratum spinosum has 5-15 layers, the Stratum granulosum has 1-3 layers and the Stratum corneum has 5-10 layers of keratinocytes. He has also explained about the morphology of the keratinocytes in different layers of the epidermis. The keratinocytes of the basal layer were found to be columnar or cuboidal with basophilic cytoplasm and a large nucleus. The basal layer also contains stem cells which were found to help in the regeneration of the

epidermis. The malphigian layer was found to contain polygonal cells with eosinophilic cytoplasm and the nucleus was vesicular. The granular keratinocytes was found to contain flattened cells with highly basophilic histidine rich proteins, the profilaggrin, keratin and keratohyaline granules. The horny layer, the Stratum corneum contains highly flattened keratinocytes with eosinophilic cytoplasm. These corneocytes was found not to contain nucleus and cytoplasmic organelles. These cells were found to play an important role in the protective barrier function of the skin.

The epidermis contained the eccrine sweat glands and sebaceous glands. So the epidermis of the adult skin was found to be thick with more number of sweat glands and sebaceous glands. Melanocytes derived from the neural crest were found in the basal layer of the epidermis. Adult skin contains more amounts of melanocytes. The number of melanocytes was found to decrease with increasing age.

The adult skin has an undulating Dermo-Epidermal junction with more number of epidermal ridges and dermal papillae. The dermis has two layers the papillary and reticular dermis. The adult skin was found to have more number of collagen and elastic fibers which provides the tensile strength and elasticity to the adult human skin.

Jane Sandby-Moller et al (2003) has measured the thickness of the Stratum corneum and the cellular epidermis. There was no variation in the thickness of the epidermis in the skin of individuals from 20 to 68 years of age. There was difference in the thickness of the Stratum corneum between sun protected body sites and sun exposed body sites. The Stratum corneum was thicker in sun exposed body sites.

Tapan K Bhattacharya (2004) has studied the percentage area of collagen and elastic fibers which determines the depth of epidermis, dermis and any variation in the pilosebaceous units and blood vessels. Atrophy of the epidermis was noted in older mice. The number of pilosebaceous units was found to be decreased in older mice. The sebaceous gland was found to be atrophied with pyknotic nuclei. The epidermis was found to be atrophied or flattened.

Neerken S et al (2004) has studied the age related changes in the skin. The thickness of the epidermis was found to be decreased and the Dermo-Epidermal junction was flattened in old age.

Jeanette M. Waller (2005) has explained that the thinning of the epidermis in old age is due to the reduction in the number of epidermal projections into the dermis resulting in flattening of the Dermo-Epidermal junction. This was found to result in tearing of the skin following minor trauma making the aged skin less resistant to shearing forces. Young skin was found to have a convoluted Dermo-Epidermal junction. This convolution persists till 60 years of age and then slowly it starts to get flattened. The thickness of the Stratum corneum of the epidermis is not altered in old age.

Chantal .O. B et al (2006) has described the aged epidermal permeability barrier. Stratum corneum contains lipid depleted cells. The lipids are in the form of ceramides, less amount of cholesterol and free fatty acids. These three fats constitute 10% of the dry weight of the Stratum corneum. Although the Stratum corneum is considered to contain dead cells, it is found to be metabolically active and interactive with underlying layers of the epidermis. The cutaneous permeability barrier is affected in aged skin. This was found to be due to the decreased proliferation of the epidermal cells and decrease in lipid synthesis. The

cell signaling pathways namely the epidermal growth factor and interleukin 1 are maintaining the normal epidermal permeability barrier.

Abnormal cytokine signaling and interleukin1 is mainly producing abnormality in the barrier functions in the aged epidermis. The changes in the aged Stratum corneum are due to interference in the hydration levels. The corneocytes enlarges in size and the lamellar network of the Stratum corneum is disorganized in aged epidermis and alters the epidermal structure and function with decrease in epidermal thickness, flattening of the Dermo-Epidermal junction etc, whereas photo aging produces increase in epidermal thickness, uneven distribution of melanocytes and some amount of cytological atypia.

Catherine P et al (2006) explain that Stratum basale contains cylindrical cells arranged in a single layer. In Stratum spinosum, the keratinocytes are polygonal with round nucleus. Stratum granulosum contains keratinocytes which are flattened and contains grains which are the kerato hyaline granules. Stratum corneum contains anucleated corneocytes. The projections of epidermis into the dermis are the epidermal ridges and the dermis into the epidermis is the dermal papillae.

The dermis has papillary and reticular dermis containing collagen, elastic and reticular fibers. With this histological picture of the layers of skin reported above, the age changes in the epidermis and dermis has been studied.

J S Pasricha (2006) says that skin being the largest organ of the body has two layers namely the epidermis and the dermis. The main cells of the epidermis are the keratinocytes. These cells are columnar in Stratum basale arranged in a single layer. Superficial to the Stratum basale is the prickly cell layer where the keratinocytes are polygonal and arranged in several layers. Superficial to this is the granular layer with rhomboid shaped keratinocytes. Most superficial layer, the Stratum corneum has anucleated cells which are fragmented and fall off from the surface. This layer protects the skin from penetration of water and allows the penetration of larger molecules. The processes of epidermopoiesis occur continuously with new cells forming in the basal layer and the old cells getting fragmented and fall off from the superficial layer. The turn over time of the epidermis is 28 days. This time is modified with injury to the skin and various skin diseases. The Stratum corneum acts as a

mechanical barrier and protects the skin from harmful invading microorganisms.

The dermis has the superficial papillary dermis and the deep reticular dermis. Collagen fibers being the major component of dermis is thin and arranged singly in papillary dermis and is thick and arranged in a criss cross pattern in reticular dermis. The dermis also contains elastic fibers which are arranged perpendicular to the epidermis in the papillary dermis and horizontally oriented, in the junction of the papillary and the reticular dermis. These collagen and elastic fibers in the dermis were found to be embedded in the ground substance which was found to be mainly made up of water and proteoglycans. The Dermo-Epidermal junction is wavy due to the epidermal projections, namely the Rete Pegs into the dermis. This Dermo- Epidermal junction was flattened with increasing age with atrophy of the epidermis.

James Varani et al (2006) have studied about the reduction in the collagen fibers in chronologically aged skin of 80 years of age by comparing with young skin of 18-29 years of age. He has explained that the reduction in the number of collagen fibers in aged individuals is due

to the reduction in the fibroblasts. The collagen fibers were found to be fragmented in older skin. This occurs due to chronic exposure to sun, which causes the up regulation of collagen degrading matrix metalloproteins. In naturally aged skin, these matrix metalloproteins are gradually up regulated causing fragmentation of the collagen fibers.

Leslie Baumann (2010) has explained the role of elastin in producing changes in old skin. Collagen and elastic fibers make up the dermis of the older skin. Elastic fibers contain oxytalan and elaunin fibers. Oxytalan fibers are the least mature fibers. They run in a perpendicular direction from the Dermo-Epidermal junction to the reticular dermis. Elaunin fibers are said to be more mature fibers and they run horizontally in the reticular dermis. These fibers make the young skin more elastic. This network formed by the elastic fibers gets reduced as age advances producing sagging of the skin.

Skin of the sun exposed areas show hyperplasia of the elastic fibers. The elastin degrades into an amorphous substance and gets accumulated in the papillary dermis. So this study says that chronological aging causes disintegration and photo aging causes thicker elastotic

fibers. Degradation of proteins producing glycation end products in the dermis is said to begin at approximately 35 years of age.

Ashok Agarwall (2007) has explained about the normal histological appearance of the layers of skin. The epidermis is thin to 0.04mm in thin skin and is thicker to 1.6mm in the palm and sole. The keratinocytes and the melanocytes are the two main cells present in the epidermis. He has said that the keratinocytes form about 90% of the cells of the epidermis. The cells of the basal layer, the Stratum basale are columnar in shape connected across each other by desmosomes.

The cells of the spinous layer are squamous cells and that of the granular layer are diamond shaped or flattened cells with keratohyaline granules. The cells of this layer take up the basophilic stain and are irregular in their size and shape. The thickness of the Stratum granulosum in normal skin is found to be proportional to the thickness of the Stratum corneum. This superficial layer is metabolically active and has flattened anucleated cells.

Melanocytes appear as clear cells between the keratinocytes of Stratum basale. Melanocytes have abundant translucent

Cytoplasm. The nucleus is small and deeply basophilic than the keratinocytes. It is said that one melanocyte makes connection with about 36 keratinocytes. The ratio of arrangement of melanocytes to the basal keratinocytes is found to be 1: 10.

The sebaceous gland has several lobules. Each lobule has an outer row containing undifferentiated, flattened cells with large nucleus and a basophilic cytoplasm. The inner portion is larger in size and has foamy pale staining cytoplasm. The nucleus is scalloped due to compression by lipid vacuoles. The sebaceous duct opening into the hair follicles is lined by squamous epithelium.

The dermis consists of non cellular connective tissue and has mostly collagen fibers and elastic fibers which are delicate branching. The dermis is found to be 15 to 40 times thicker than the epidermis, with the thickness varying according to the site of the skin. The two layers of the dermis is the papillary dermis, which is the thin zone and reticular dermis, which is the thick zone. The collagen fibers in the dermis are arranged as thick bundles and the elastic fibers are found to be thinner and wavy than collagen fibers and the elastic fibers are found to be twisted around the collagen fibers.

David H Chu (2008) has explained the histological features of aged skin. The changes noted in the epidermis were decrease in the thickness of the epidermis, flattening of the Dermo-Epidermal junction and variable size and shape of the keratinocytes. The number of melanocytes was also reduced.

Atrophy of the dermis was noted due to the decrease in the collagen and elastic fibers of the dermis. The number of sweat glands was found to be reduced. All these microscopic changes noted in the older skin were the reason for the dryness, wrinkling and laxity of the skin. In photo aged skin the Stratum corneum was more compact, granular cell layer was thicker, but the overall epidermal thickness was reduced. The number of melanocytes was increased and there was hyperplasia of the sebaceous glands. Fragmented collagen and elastic fibers was noted in the dermis.

Susan Standring (2008) explains that the skin of a neonate appears to be thinner than the skin of an older infant and children. The cornified layer which provides protection to the skin takes a period of 2-3wks to get cornified. Various environmental and chronological factors influence

aging of skin. Sun is the major environmental factor influencing the age changes in the skin. Changes in the skin start to appear from the third decade of life. Normally there is epidermal and dermal atrophy.

Flattening of the skin affects the nutrition to epidermis by reducing the contact area between epidermis and dermis causing poor adhesion to epidermis.

The dermis gets separated from epidermis even with minor injury. No change is found in the thickness of the cornified layer in old age. So the permeability seems to be little affected. The rate of epidermal cell replacement decreases to 50% in old age. The number of melanocytes decreases to 10-20% after middle age. The cellularity of the skin is reduced. Dermis also shows many changes like reduced collagen synthesis which will be reflected externally as stiffness. Senile elastosis appears as age advances and produces wrinkling and flaccidity of the skin. The vascularity of the skin is reduced. This makes the cutaneous vascularity more fragile and increased tendency towards appearance of small purpuric spots.

M. Dumas et al (2008) have studied the influence of age and exposure to sunlight on the skin. The epidermis was found to be thinner with increasing age with a difference of 5 micrometers with each decade. He has reported that the decrease in the epidermal thickness is due to the reduction in the number of layers of keratinocytes. The thickness of the Stratum corneum was found to remain unaltered with increasing age. The rate of cell turnover was found to be decreased in the epidermis of aged individuals and the Dermo-Epidermal junction was found to be flattened. This was found to occur due to the reduction in 2 regulatory proteins namely, P63 which was found to be involved in maintaining the proliferative activity of the basal keratinocytes and beta 1 integrin, which is an adhesion protein found in the basal keratinocytes. The transepidermal water loss was found to be controlled by Stratum corneum maintaining the osmotic equilibrium within the epidermis. Thus the hydration was found to be controlled by aquaglyceroporin3. These proteins were found to be present in the plasma membrane of the keratinocytes found throughout the epidermis. This aquaglyceroporin3 was found to be decreased in aged individuals. But no significant

difference was found in the AQP3 between sun exposed and unexposed areas of the skin.

Yolanda R H (2008) explains about the signs of aging and photo aging. In chronological aging skin, the epidermis was found to be atrophic due to thinning of the epidermis, loss of Rete Pegs and flattening of the Dermo-Epidermal junction. Collagen is considered to be the building blocks, which mainly provides strength to the human skin. Transforming growth factor-beta and Activator protein-1 are found to be the two regulators of collagen production. TGF-beta was found to promote collagen formation while AP-1 was found to promote collagen break down by up regulating matrix metalloproteinases. With chronic exposure to sunlight these matrix metalloproteinases are up regulated which were found to result in increased degradation of collagen. The sun exposed areas of the aged skin was also found to have almost the similar findings as in the chronologically aged skin except for the number of melanocytes which was found to be increased in the photo aged skin.

Gandhi A et al (2009) has reported the histological changes in aging and photo aging. The aging skin showed reduction in the thickness of the epidermis. The collagen fibers and the elastic fibers in the papillary dermis also got reduced. The reduction in the number of elastic fibers in older person was found to be reflected externally as wrinkles. Photo aged skin also showed almost the similar changes in the epidermis and dermis except for the increase in the number of melanocytes of the basal layer of the epidermis of photo aged skin. All these changes makes the aged skin susceptible to various skin diseases especially xerosis and pruritis.

Arun C Inamadar (2009) explains the development of the skin. Gastrulation occurs in 3 weeks following fertilization and the three germ layers namely the ectoderm, endoderm and mesoderm are formed. Then the ectoderm divides into neuroectoderm and presumptive epidermis. At about 30 days of gestation the formation of skin becomes evident. The epidermis, the dermis and the Dermo-Epidermal junction with the blood vessels and nerves become apparent by about 6 weeks. The epidermis has initially only two layers, the basal cellular layer and periderm cells. This periderm gets differentiated into adult epidermis. Melanocytes appear by 50 days but lack melanosomes.

The skin appendages were not found at this stage. Around 80 days of gestational age melanocytes are found with maximum density. The melanosomes appear by late first trimester. The epidermis had three layers at this stage. The melanocytes transfer the pigment to the adjacent keratinocytes in the fifth month of gestation. Dermis shows the appearance of elastic fibers of adult skin in the second trimester. During the third trimester the epidermis gets fully organized into all five layers and assumes the adult type. The skin of a newborn shows flattening of Dermo-Epidermal junction with well developed skin appendages. So the adult skin structure develops by third trimester and it undergoes changes in the thickness of the epidermis, Dermo-Epidermal junction and in the cellularity and vascularity with increasing age.

David E. Elder (2010) has explained the development and the normal histological appearance of the layers of the skin. The epidermis begins to develop as a single layer, first as ectodermal cells. By 5 weeks it gets differentiated into two layers, the Stratum germinativum and the periderm. By next 1 week Stratum intermedium develops. By 19 weeks the cells in the periderm gets flattened. By 23 weeks the keratinocytes are well developed. Out of the five layers the Stratum basale has a single

layer of flattened cells with more basophilic cytoplasm. They contain melanocytes which transfer the pigment melanin to the adjacent keratinocytes.

The Stratum spinosum contains polyhedral cells of 5 to 10 layers which are united to each other by desmosomes. The Stratum granulosum contains flattened cells of more than 10 layers and the cytoplasm of these cells contains keratohyaline granules. The Stratum corneum contains anucleated cells. The melanocytes are derived from the neural crest and they are found in the Stratum basale. These are the dendritic cells. The dendrites cannot be seen in Haematoxylin and Eosin stain. They can be identified with their round or oval dark staining nuclei with a clear halo of surrounding cytoplasm. They are found in the ratio of 1 to 10 keratinocytes in the Stratum basale. The number and the size of the melanocytes are found to increase in sun exposed skin.

The eccrine glands are found to develop first in palms and soles by fourth month of gestational age and they appear in the remaining areas of the body by fifth month. The dermis has two layers the papillary and the reticular dermis. The papillary dermis represents the thin zone and the reticular dermis the thick zone. Both the layers of the epidermis can be identified by the presence of collagen, elastic and reticular fibers.

The layers of the skin can be identified with the above mentioned histological appearance.

As age advances the thinning of the epidermis can be noted with flattening of the Dermo-Epidermal junction. The number of melanocytes decreases with increasing age, but in sun exposed skin the number of melanocytes increases. Dermis shows atrophy with decrease in the collagen and elastic fibers. Sweat glands were decreased and there was no change or increase in the size of the sebaceous glands with increasing age.

Thomas P. Habif (2010) has explained about normal aging and photo aging. The normal aging starts to get reflected externally by 30-35 years of age. The skin of the aged individuals is found to be thin and fragile. The epidermis becomes thin. The vascularity is reduced. The number of collagen and elastic fibers of the dermis is reduced. The number of sweat glands and sebaceous glands is also found to be reduced. Fine wrinkles appear in the skin like crumples of cigarette paper which is due to the loss and fragmentation of elastic fibers.

In aged skin in sun exposed areas, the epidermal thickness increases. Chronically sun exposed children have significant actinic damage by age of 15years. These features become apparent over the skin by 20years of age. Sun exposure mainly affects the elastic fibers forming elastosis which is characterized by deposition of yellow amorphous elastic material over the upper dermis which do not constitute the functional elastic fibers.

Giangreco A et al (2010) have reported the changes in the epidermis with increasing age in 3 different age groups. This study has reported that, the thickness of the epidermis decreases with increasing age resulting in decreased proliferative activity of the epidermis, the height of the Rete Ridges also decreases and the density of the basal cells markedly decreases in persons more than 60years of age. The height of the Rete ridges was found to be decreased in individuals from 50-59 years of age and also in individuals of more than 60 years of age.

Langton A. K et al (2010) have studied the roll of elastic fibers causing changes in the aged skin. They have studied that the intrinsic

changes in the aged skin are a slow process. With increasing age there is atrophy of the epidermis and dermis. The number of fibroblasts is reduced thereby the collagen fibers are reduced in aged skin. The surface area of the Dermo-Epidermal junction is reduced in subjects from 21-40 years of age and almost flattened in 61 to 80 years of age. This flattening makes the skin more fragile due to decrease in the transfer of nutrients between the epidermis and dermis.

In photo aged skin the epidermis undergoes atrophy, but the effects of sun exposure are more pronounced in elastic fibers of the dermis. The initial changes observed due to photo damage are hyperplasia of the elastic fibers with accumulation of amorphous elastin material. Degenerative changes are noted in the oxytalan fibers at the Dermo-Epidermal junction. This manifests as loss of skin elasticity and wrinkles of skin.

Brian J. Hall (2010) has described the structure of the skin with its appendages. The Stratum basale, the lowermost layer of the epidermis was considered as the stem cell layer. The normal cell turnover time is 3-4 weeks. The Stratum spinosum is made up of several layers of polyhedral

keratinocytes. Stratum granulosum has flattened keratinocytes with kerato-hyaline granules in their cytoplasm. Outermost layer, the Stratum corneum is the keratin layer made up of stratified layers of dead keratinocytes. Beneath the Stratum basale is the Dermo-Epidermal junction, which undergoes changes in old age with loss of Rete Pegs, leading to the flattening of the Dermo-Epidermal junction which appears convoluted in young skin. Melanocytes can be identified in the Stratum basale as small cells with dark staining nuclei and clear cytoplasm. They occupy 10% of the total cells in Stratum basale. The dermis has two layers the papillary and the reticular dermis with the skin appendages within it namely, the sweat glands and the sebaceous glands. In aged skin the dermis was atrophied, the number of melanocytes was found to be decreased. The number of sweat glands was found to be reduced and the sebaceous glands showed increase in size. The number of sebaceous glands was not altered in aged skin.

Yu Liu et al (2010) have compared the skin of bama minipig with the human skin. The bama minipig was found to have the same structure like the human skin and showed the same features like humans with increasing age like decrease in the thickness of the epidermis, flattening

of the Dermo-Epidermal junction, except for the vascular system which was underdeveloped in bama minipigs

Malvi (2011) has studied the flattened Dermo-Epidermal junction in aged epidermis. The thickness of the epidermis was found to be greater in sun exposed areas. This epidermal atrophy and decreased cell turn over in the Stratum corneum renders the skin a rough and dull surface. 20% of the dermal thickness is found to disappear in older adults. The Dermo-Epidermal junction contains type 4 collagen, which provides the structural framework and mechanical stability. So as age advances the Dermo-Epidermal junction flattens and contributes to wrinkle formation.

Collagen type 7 is the basic component of anchoring fibrils. These anchoring fibrils attach the basement membrane zone to the underlying papillary dermis. These anchoring fibrils are found to be decreased in chronically sun exposed than sun protected areas. Sun exposed skin shows thickening and coiling of elastic fibers in papillary dermis. This study says that the age related changes in elastin is not well understood as that of the changes in collagen. The sagging skin in older individuals may be due to the loss of elasticity.

Kakasheva-Mazhenkovaska L et al (2011) has studied the histological changes of skin in 5 age groups namely up to 1year, 2-12years, 13-22, 23-55 and 56-73years of age. Thickness of the epidermis, changes in the Dermo-Epidermal junction and the skin appendages has been studied. Thickness of the epidermis was found to be reduced in the 5th group; with flattening of the Dermo-Epidermal junction and decrease in the number of sweat glands and sebaceous glands.

Lawrence A Schachner (2011) explains the development of the skin and about the structural and functional changes in the skin of the infants, children and adults. The skin appendages namely the sweat glands and sebaceous glands become apparent by 12-14weeks of gestational age. The functions of the skin depend mainly on the two tissues, the epidermis and the dermis.

The epidermal appendages and the blood vessels provide nutrition to the skin and integrate the epidermis and dermis. The epidermis is highly cellular and the dermis is almost acellular with more extracellular matrix like collagen and elastic fibers. The epidermis is the

regenerating living barrier which responds to various external and internal stimuli continuously. The thickness of the epidermis is 0.4mm to 1.5mm in thin skin and 1.5 to 4mm in palms and soles where it is thick. The innermost layer, the Stratum basale contains stem cells which differentiates and gives rise to keratinocytes to the other layers above it. The keratinocytes are ectodermal in origin accounting for 80% of the cells in the epidermis. These cells regulate the exchange of water and gas across the epidermis and form an epidermal protective barrier. The proliferative time of the keratinocytes from the basal layer to the Stratum corneum is 14 days.

The Stratum spinosum has spinous cells. The spines are the desmosomes. These are the structures which provide resistance to mechanical stress. These contain the protein desmoglein 1, 2 and 3. Auto antibodies are produced against desmoglein 3, which produces disruption of the epidermis leading to a condition called Pemphigus vulgaris. These desmosomes are calcium dependant. So calcium is the mediator of adhesion between the cells in Stratum spinosum. Mutations in the genes that regulate the calcium transport produces diseases like Darriers disease and Hailey Hailey disease. The cells in Stratum granulosum has highly convoluted nucleus which is a characteristic feature of early stages of

apoptosis. The keratohyaline granules contain profilaggrin, loricin and keratin filaments. Mutations in the genes coding for filaggrin and loricin leads to diseases like Ichthyosis Vulgaris and Vohwinkels syndrome. This explains the importance of this cornified envelope in normal epidermis.

Stratum corneum is called dead epidermis because it contains anucleated flattened cornified cells. Thickness of the Stratum corneum is same in the infants and adults. The papillary dermis is no more than twice the thickness of the epidermis and the reticular dermis forms the main bulk of the dermis. During development the dermis interacts in the morphogenesis of epidermal appendages and Dermo-Epidermal junction. It also interacts in repair and remodeling of skin following a wound.

Kakasheva-Mazhenkovaska L et al (2011) have studied the histological changes in the capitulum of subjects of 3 age groups namely during the first year, puberty and adolescence and beyond 55years. The thickness of the epidermis was maximum by 22years and was found to decline gradually from 55years beyond which it reaches the thickness of the epidermis as it was in childhood. All the structural components of the

skin becomes established under the influence of sex hormones from the puberty period.

The Dermo-Epidermal junction gets flattened because of the fragmentation of vertically placed elastic fibers becoming horizontal in position. This study explains that the concentration of elastic fibers in the dermis increasing with age may be due to the decrease in the percentage of collagen component. Since this finding is contradictory from the findings in other literatures, it was explained as due to the decrease in the peripheral fibrillin component of the elastic fibers with accumulation of abnormal elastic fibers. The various parameters of the skin measured in children to older individuals did not show any significant variation in relation to sex of an individual.

Karine cucumel et al (2012) has explained the cutaneous aging by measuring the parameters of skin using confocal laser scanning microscope. In 40-50years age group, the retraction of the Rete Pegs has been found out which leads to flattening of the Dermo-Epidermal junction. In the group of 50-60years the Dermo-Epidermal junction was completely flattened with absence of Rete Pegs. The density of the

papillary dermis was found to be decreased in this age group due to decrease in density of the collagen fibers.

Similar changes in the structure of the epidermis and dermis was noted in the group of 60-70years of age. This literature has given the explanation for these changes as, the aged epidermis shows resistance to shearing force and reduced vascularity in aged persons also leads to poor nutrition of the basal cells.

Alexandra L et al (2012) have studied the age related skin changes in individuals from 17 to 81 years of age. The changes in the skin start to appear before 30years of age. They have studied the changes in the dermis leading to degeneration in the connective tissue of the dermis namely collagen and elastic fibers with reduction in the hydration of the dermis. Chronic exposure to sunlight produces increased elastosis.

With increasing age the lifespan of the fibroblasts of the dermis and their capacity to divide is also reduced and so the collagen production is reduced. As age advances there is increased production of chondroitin sulphate and decreased production of dermatan sulphate, so

there is increase in the synthesis and enlargement of collagen fibrils. This reduces the elasticity of the skin.

Photo oxidative damage results in decrease in the tensile strength and stability of the skin. There is reduction in the thickness of the epidermis. Accumulation of keratohyaline granules in the Stratum granulosum has been noted. The Dermo-Epidermal junction flattens due to reduction in the number of dermal papillae and epidermal buds. Reduction in the collagen fibers of the dermis leads to wrinkle formation.

May F Al Habib (2012) have studied the aging effects of human skin with wrinkles. The individuals has been divided into three groups of Group A (1-9years), Group B (12-30years) and Group C (40years and above). In Group A the layers of the epidermis were identified separately. The thickness of the Stratum corneum was found to be decreased. The collagen fibers in the dermis were disorganized. The cellularity was found to be decreased and the skin appendages were diminished. In Group B the epidermal layer was found to be thick and the dermal papillae were well organized. The number and the depth of the dermal papillae were increased.

The collagen fibers were thick with uniform and parallel arrangement. The skin appendages appeared distinct. In Group C, the epidermal thickness was reduced. The number of dermal papillae was decreased and the depth of the papillae was shallow. There was not much difference in the number of melanocytes between the younger and adult age group. But marked decrease in the number of melanocytes was found in older age group. So the number of melanocytes and its capacity to produce melanosomes is affected in old people.

Carrie Sussman (2012) explains that Stratum corneum performs the main barrier function. The hydration and the lubrication of this layer have to be maintained to keep the skin intact. Excessive dryness or hydration is damaging to the skin. The barrier function of the normal adult skin can be recovered within 6 hours following an insult. But this recovery is slowed down in aged skin. The histological changes in the layers of the skin were noted from the fourth decade of life. Age related changes were atrophy of the epidermis.

Epidermis was found to become more transparent and thinned out. Thickening of the Stratum corneum and thinning of the

Stratum spinosum was noted. The proliferative activity of the keratinocytes was found to be decreased. Dermis showed changes like destruction of the collagen and elastic fibers in old age.

Kumar N et al (2012) has explained the changes in the collagen and elastic fibers of the dermis with increasing age and different sites of the body.

Nagwa H Abd El-Aal et al (2012) has studied the epidermal thickness and the changes in the collagen and elastic fibers in unexposed skin of aged and young persons. Decrease in the thickness of the epidermis was noted in old skin compared to young skin and flattening of the Dermo-Epidermal junction was also identified in old skin. Using Masson trichrome stain the collagen fibers were studied. The collagen bundles was found to be thick in young skin and thin and loosely packed in aged skin.

With orcein stain for elastic fibers, young skin had more elastic fibers and old skin had thin, fragmented elastic fibers. This study has concluded that aging changes starts appearing by 40years of age. The

decrease in the collagen and elastic fibers gives the skin a more aged appearance making the skin more fragile. The decrease in the thickness of the epidermis in older age group may be due to the decrease in the proliferation of cells in the basal layer and fas-mediated apoptosis of the keratinocytes in the Stratum spinosum and Stratum basale.

Marinela Bonta et al (2013) have found out that the changes start to appear in the dermis from 50 years of age. The fibers in the dermis were found to be loosely arranged. The collagen fibers of the superficial dermis undergo fragmentation leading to thinning of the dermis and gradually the collagen fibers in the deep dermis also undergoes fragmentation. In 75 to 80 years age group, the collagen fibers were found to be thicker but were found to be less compactly arranged. The number of collagen fibers decreases but the density of the fibers increases. The collagen fibers becomes thicker and thicker at 70 years of age and gradually becomes fibrous.

Elastic fibers become fragmented in older age group. The elastic fibers become more distorted by the process of elastolysis and

gradually disappear over 70 years of age. So these changes in the collagen and elastic fibers lead to thinning of the dermis in older groups.

Walters Kluver (2013) has explained that aged skin should be considered as a differential diagnosis for atrophic dermatitis because aged skin, particularly in those areas of skin chronically exposed to sun has showed the feature of actinic elastosis. Actinic elastosis is the distorted elastic fibers in the superficial dermis found in the aged skin.

Christos C. Z et al (2014) reported that there is deep relationship between the changes occurring in the skin with increasing age and various skin diseases. These changes occurring in the skin are said to be the signs of various skin diseases thereby helping in prevention and early diagnosis of systemic diseases. The skin weighs about 12-16% of the total human body weight. The exposed areas of the body namely the face, neck and arms are affected by various extrinsic factors and hence resulting in premature aging of the skin. The non-exposed areas of the skin are influenced by various intrinsic factors like genetic and endocrine factors. It's reported that the epidermis gets thinned out, the Stratum spinosum of

the epidermis undergoes atrophy, the Dermo-Epidermal junction is flattened and the thickness of the dermis gets reduced because of the reduction and distortion of the collagen and elastic fibers.

The skin appendages, mainly the sweat glands and the sebaceous glands get reduced and hence their function is also reduced and affected. All these intrinsic changes are reflected externally as loss of skin elasticity and the time taken for wound healing increases to 50%. So there are various skin diseases manifesting in old age namely Pemphigus vulgaris in 50-71 years of age and Bullous pemphigoid in 80 years of age. Chronic sun exposure predisposes the skin to various skin tumors like basal cell carcinoma or cutaneous squamous cell carcinoma, the features of which gets manifested in old age. All these changes were found to affect the permeability barrier of the skin.

MATERIALS AND METHODS

MATERIALS AND METHODS

Skin was obtained from the plastic surgery department in 10% formalin bottle. Normal skin was obtained from both males and females from 3 years to 75 years of age from different parts of the body except palm and sole.

The specimens were fixed in formalin for 24 hours.

Processed in series of alcoholic changes and xylene.

The specimen was dehydrated by placing it in wax in the incubator overnight

Embedded in wax

Blocks were prepared.

Then the blocks were cut in microtome of 0.4 microns thickness and placed in glass slide.

The slides were placed in incubator overnight for removal of wax.

The next day the slides were stained with Haematoxylin and Eosin by the following procedure.

1. The slides were placed in xylene for 30minutes for dewaxing.
2. Slides were hydrated in series of alcoholic changes for 1minute each, in absolute alcohol, 90%, 70% and 50% alcohol.
3. Then slides were placed in running tap water for 10 minutes.
4. Then stained with Haematoxylin for 3 minutes.
5. Rinsed in running water.
6. Differentiated in 0.3% acid alcohol.
7. Rinsed in running tap water for 10 minutes.
8. Stained with Eosin.
9. Dehydrated in absolute alcohol.
10. Cleared in xylene with alcohol and mounted.

Few set of slides were stained using special stain, Verhoeff Van Gieson stain in the following manner.

1. The slides were deparaffinised in 2 series of changes in xylene each of 15 minutes duration.
2. Hydrated in series of alcoholic changes for 1 minute, first in absolute alcohol, 90%, 70% and 50% alcohol.
3. Washed in tap water.
4. Stained with Verhoeff Haematoxylin for 10-15 minutes.
5. Washed with absolute alcohol.
6. Differentiated in 2% ferric chloride and checked in the microscope for black fibers on a dark background.
7. Rinsed in tap water.
8. Counterstained in Van Gieson stain for 2-3 minutes.
9. Dehydrated in absolute alcohol.
10. Cleared in xylene and mounted on a cover slip.

The slides were stained with Haematoxylin and Eosin and were observed for changes in the thickness of the epidermis, the number and the depth of the Rete Pegs and the nature of the Dermo-Epidermal junction.

The changes in the number and the size of the sweat glands were noted with increasing age and the changes in the number and the arrangement and distribution of the sebaceous Glands were also noted.

The slides were stained with Verhoeff Van Gieson stain and the changes in the density and the structure of the elastic fibers and the collagen fibers were noted.

OBSERVATIONS

OBSERVATIONS

The changes in the skin with increasing age are a complex process. The structural changes lead to disturbances in the functions of the skin, making the skin susceptible to various diseases. So microscopic structural changes in the layers of the skin were studied by grouping the individuals in 4 age groups.

Group A: Skin specimens from 5 persons of 3 to 20 years of age of which 2 specimens were from females and 4 from males.

Group B: Skin specimens from 12 persons of 21 to 50 years of age of which 3 specimens were from females and 9 were from males.

Group C: Skin specimens from 8 persons of 51 to 65 years of age of which 5 specimens were from females and 3 specimens were from males.

Group D: Skin specimens from 4 persons of more than 65 years of which 3 specimens were from females and 1 from male.

The microscopic changes in the epidermis, Dermo-Epidermal junction and the number and the depth of Rete Pegs were observed in the Haematoxylin and Eosin stained slides. The epidermal thickness was

measured and analyzed using the computer system for image processing and analyses and light microscope using 10X in micrometers.

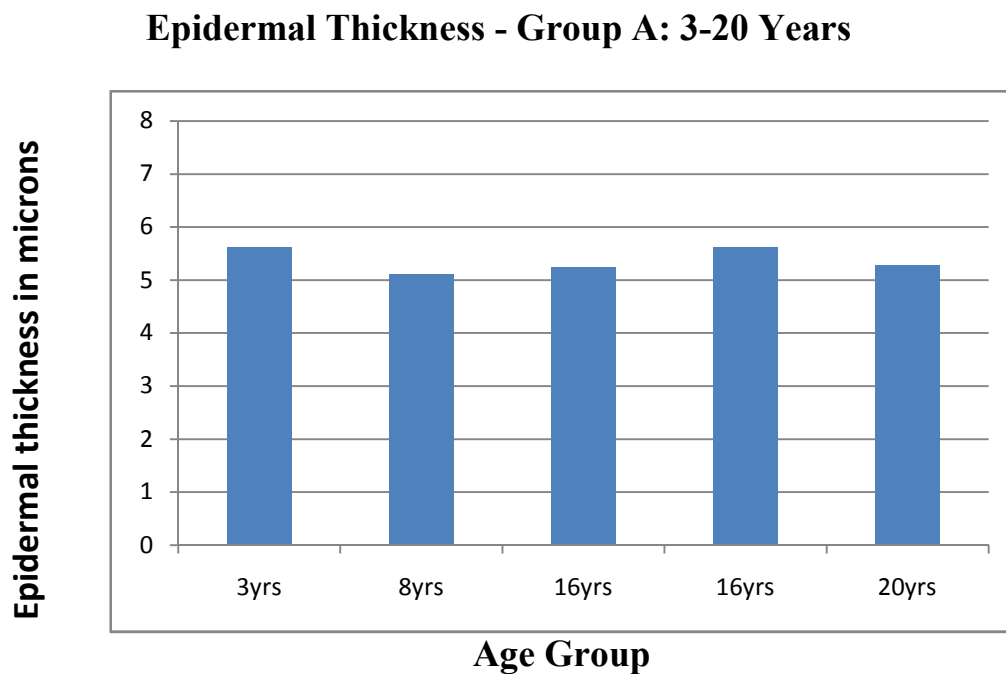
EPIDERMAL THICKNESS: GROUP A: 3-20Years

The thickness of the epidermis among Group A individuals between 3-20 years of age was as found in Table 1. The mean thickness of the epidermis was 5.37micrometers.

Table: 1

AGE IN YEARS	EPIDERMAL THICKNESS IN MICROMETERS
3	5.62
8	5.11
16	5.23
16	5.62
20	5.27

The epidermal thickness among Group A persons from 3-20years of age is represented as bar diagram.



RETE PEGS AND DERMO-EPIDERMAL JUNCTION: GROUP A

There were about 11 Rete Pegs in a field as in Fig (1). The depth of the Rete Pegs was more compared to group B individuals as in Fig (2).

Dermo-Epidermal junction was convoluted as in Fig (2) and Fig (3).

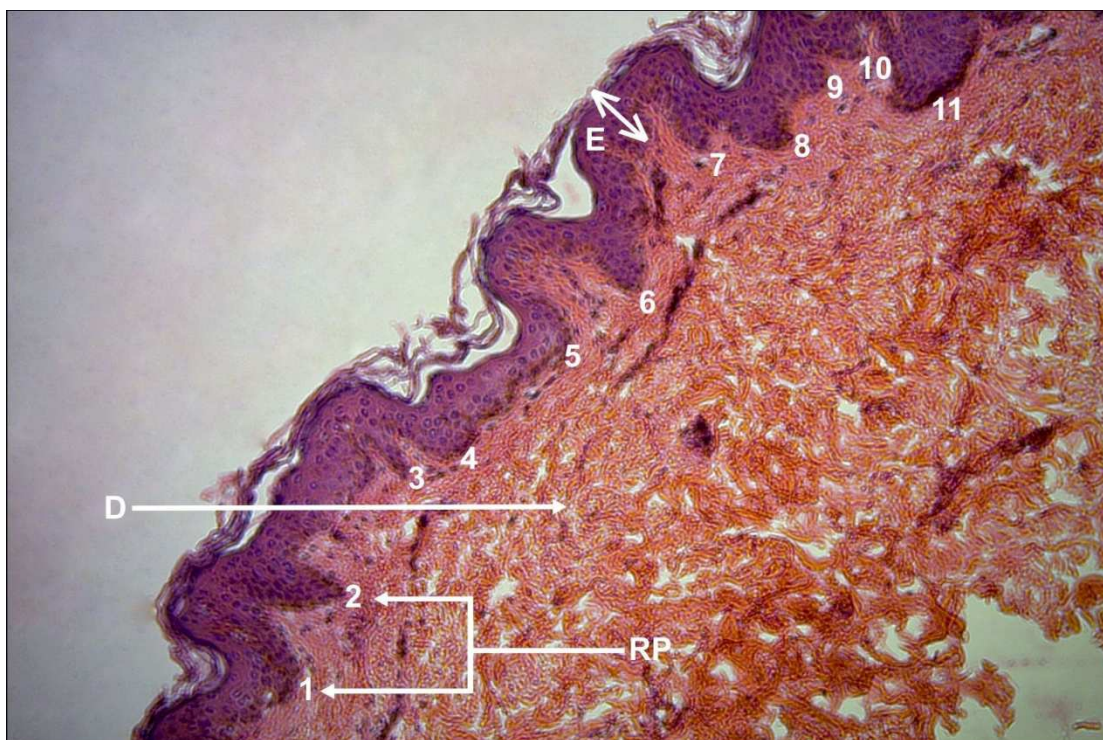


Figure 1: Group A : 3-20 Years (10x X 10)
E : Epidermis (Thin) D : Dermis RP : 11 Rete Pegs

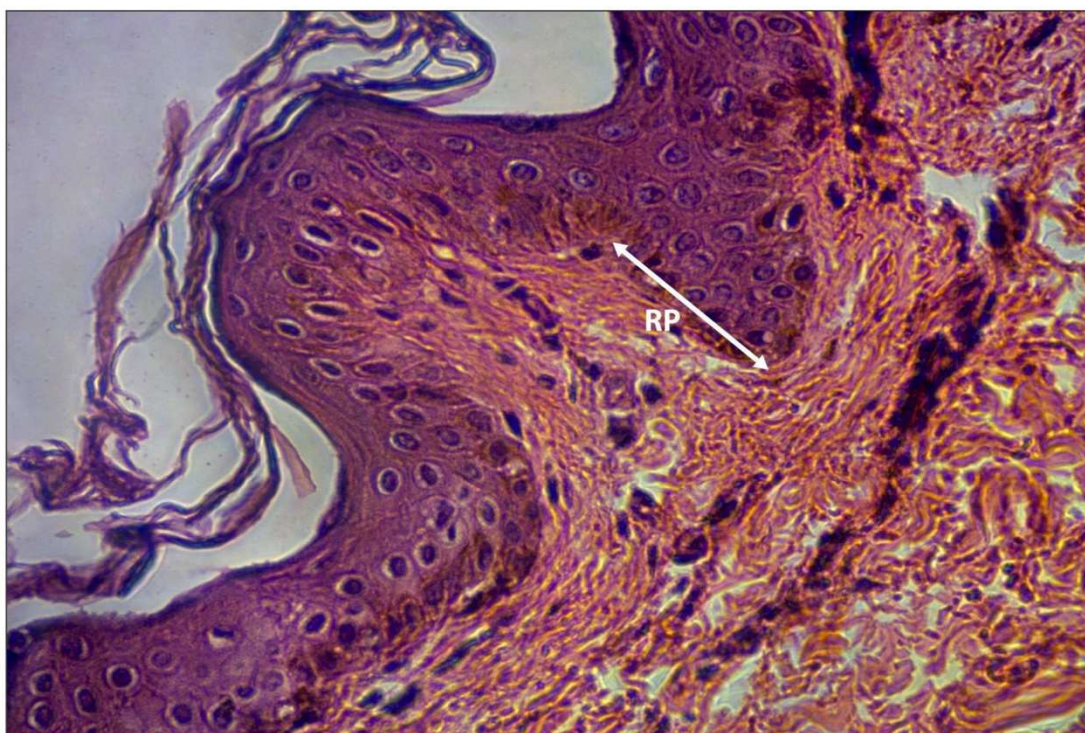


Figure 2: Group A : 3-20 Years (10x X 40)
RP : Rete Pegs (Deep)

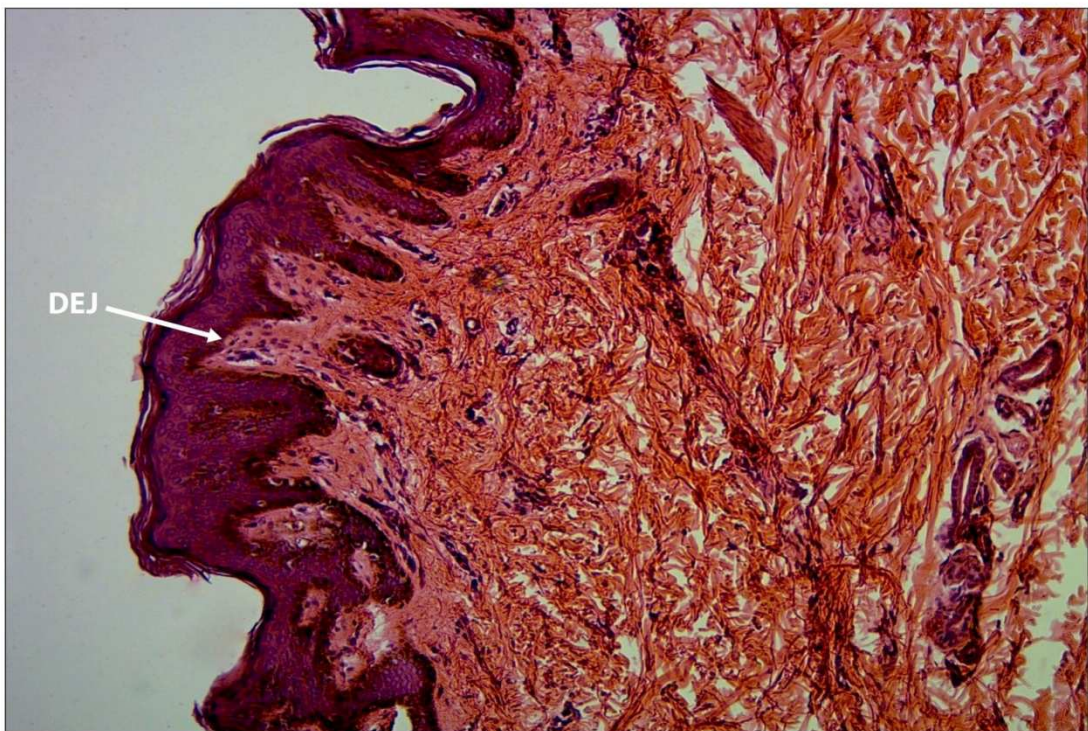


Figure 3: Group A : 3-20 Years (10x X 10)
DEJ : Dermo - Epidermal Junction (Highly Convoluted)

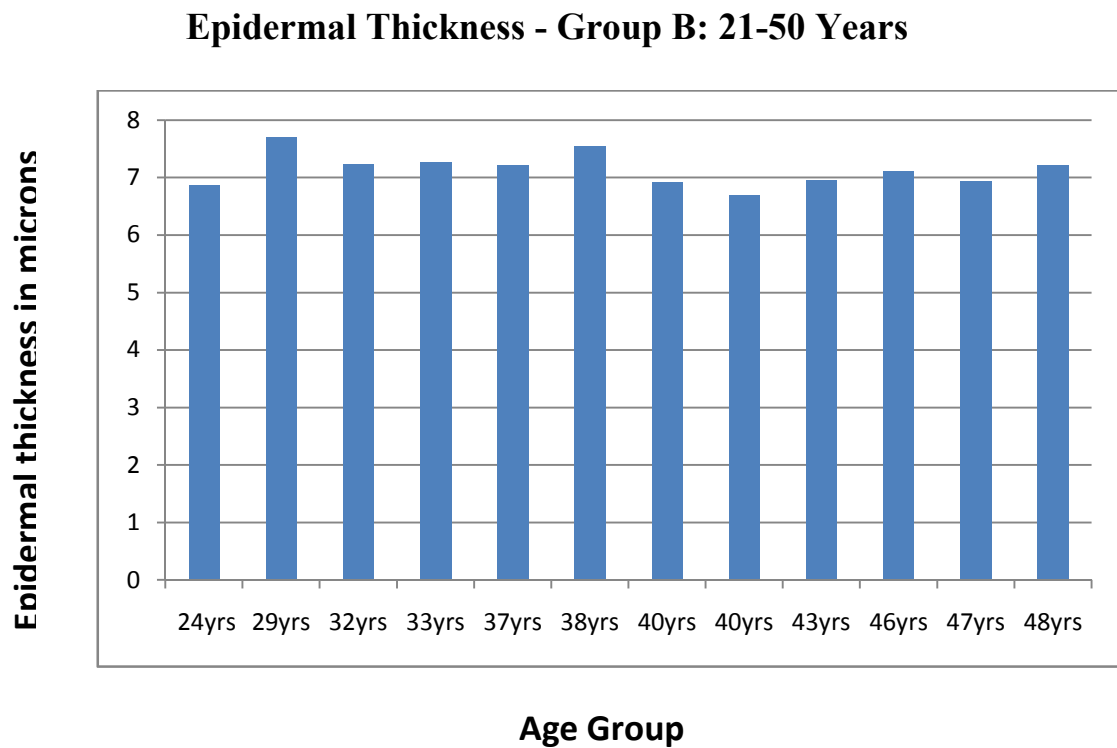
EPIDERMAL THICKNESS: GROUP B: 21-50Years

The thickness of the epidermis among Group B individuals from 21-50 years of age was as found in Table 2. The mean epidermal thickness was 7.09 micrometers.

Table: 2

AGE IN YEARS	EPIDERMAL THICKNESS IN MICROMETERS
24	6.86
29	7.69
32	7.23
33	7.26
37	7.21
38	7.54
40	6.91
40	6.69
43	6.95
46	7.10
47	6.94
48	7.21

The epidermal thickness among Group B persons is represented as bar diagram



MEAN EPIDERMAL THICKNESS: GROUP B

The mean epidermal thickness among Group B individuals from 21-30years, 31-40years and 41-50 years was as found in Table 3 in which no significant difference was observed.

Table: 3

AGE GROUP IN YEARS	THICKNESS OF THE EPIDERMIS IN MICROMETERS
21-30	7.8
31-40	7.15
41-50	7.05

RETE PEGS AND DERMO-EPIDERMAL JUNCTION: GROUP B

The average number of Rete Pegs among Group B individuals from 21-50years of age was as found in the following Table 4.

Table: 4

AGE GROUP (in years)	NUMBER OF RETE PEGS	FIGURE NUMBER
21 – 30	11	Fig (4)
31 – 40	8	Fig (6)
41 – 50	6	Fig (8)

The number of Rete Pegs was more and the depth of the Rete Pegs of Group B from 21-30 years was similar to Group A persons from 3-20years as found in Fig (4) and fig (5) and the Dermo-Epidermal junction was convoluted similar to Group A individuals from 3-20years of age as found in Fig (4). In Group B persons from 31- 40 years of age number of Rete Pegs was reduced as noted in Fig (6) and the depth of the Rete Pegs was more as found in Fig (7). In Group B from 41-50 years also the number of Rete Pegs was found to be reduced, but the Dermo-Epidermal junction was convoluted as found in Fig (8) and Fig (9).

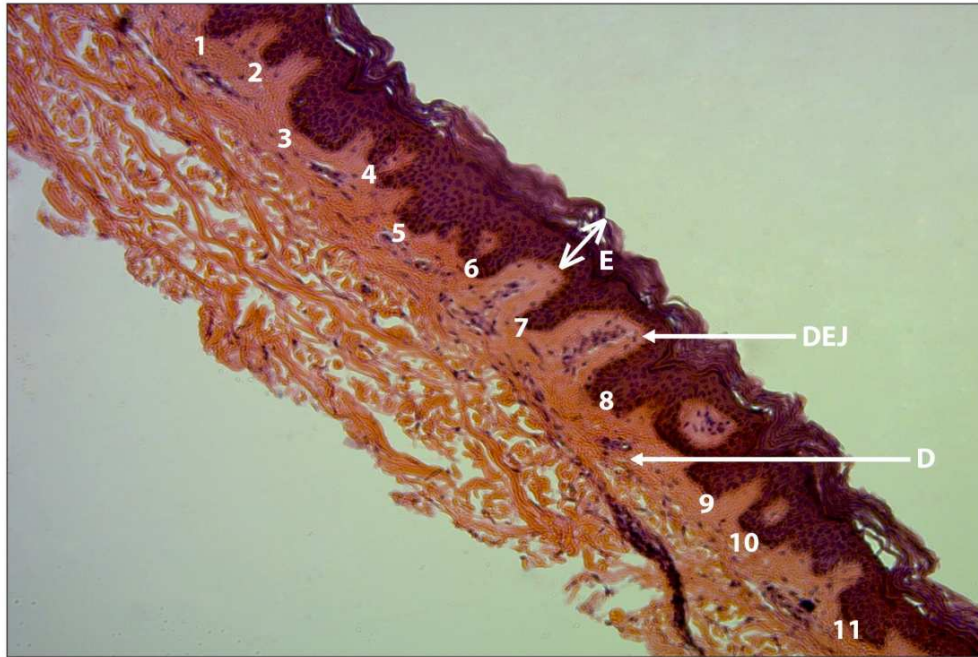


Figure 4 : Group B : 21-30 Years (10x X 10)

E : Epidermis (Thick) D : Dermis DEJ : Dermo - Epidermal Junction (Highly Convoluted)

RP : 11 Rete Pegs

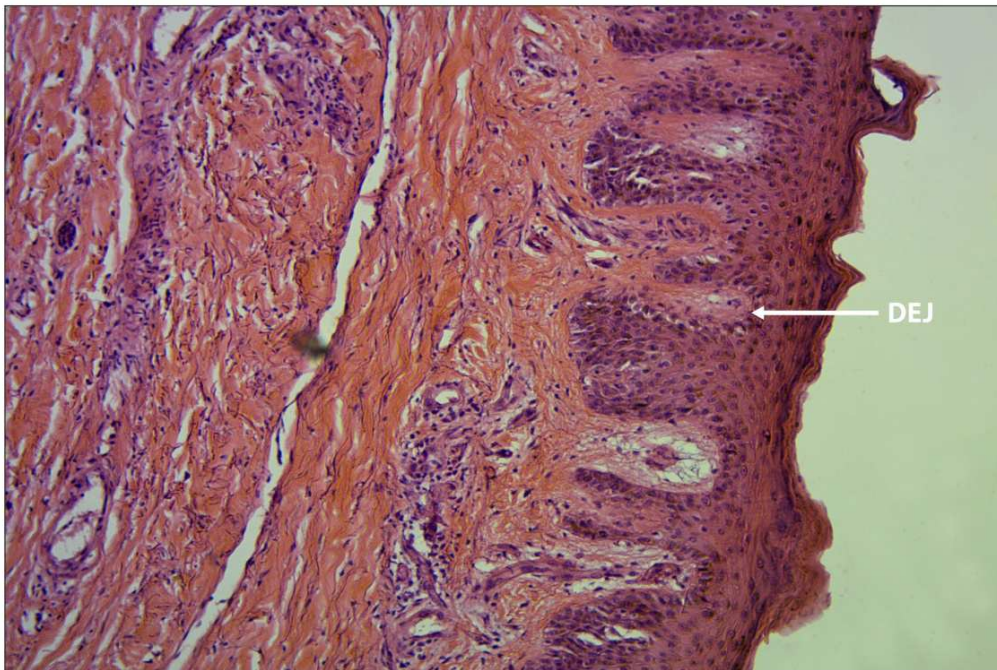


Figure 5 : Group B : 21-30 Years (10x X 40)

DEJ : Dermo - Epidermal Junction (Highly Convoluted)

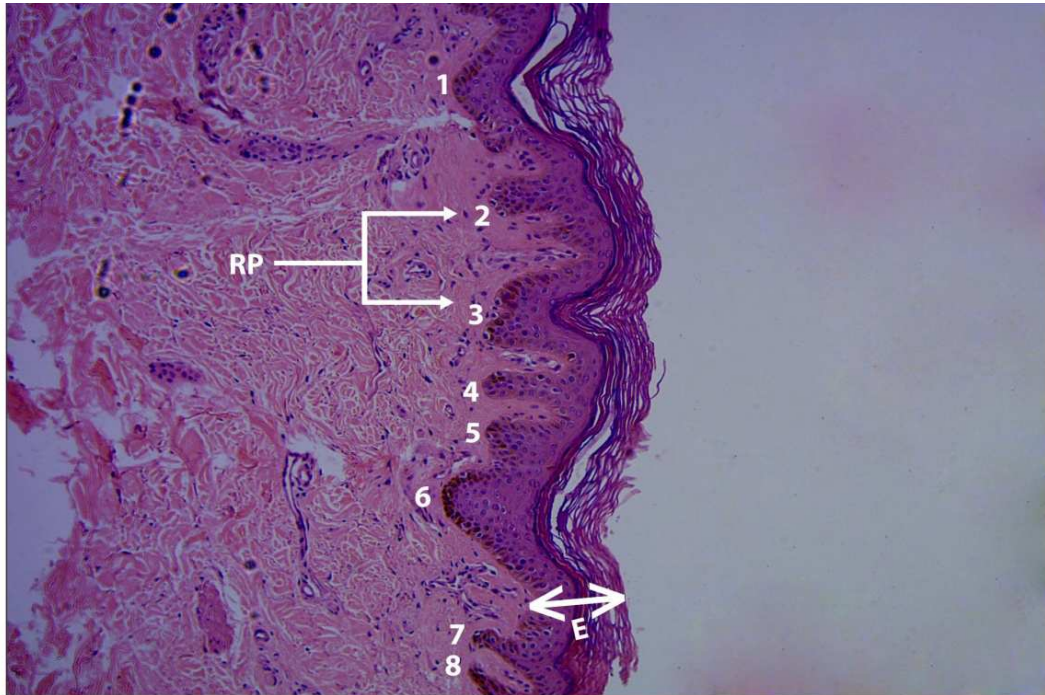


Figure 6 : Group B : 31- 40 Years (10x X 10)
RP : 8 Rete Pegs E : Epidermis (Thick)

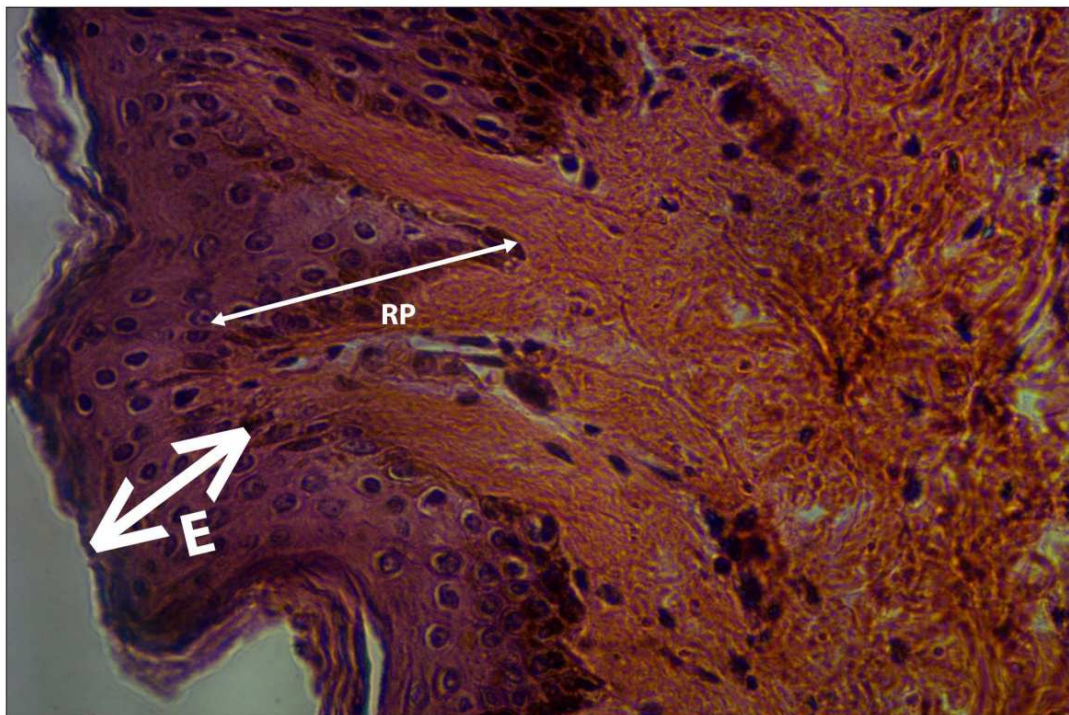


Figure 7 : Group B : 31- 40 Years (10x X 40)
RP : Rete Pegs (Deep) E : Epidermis (Thick)

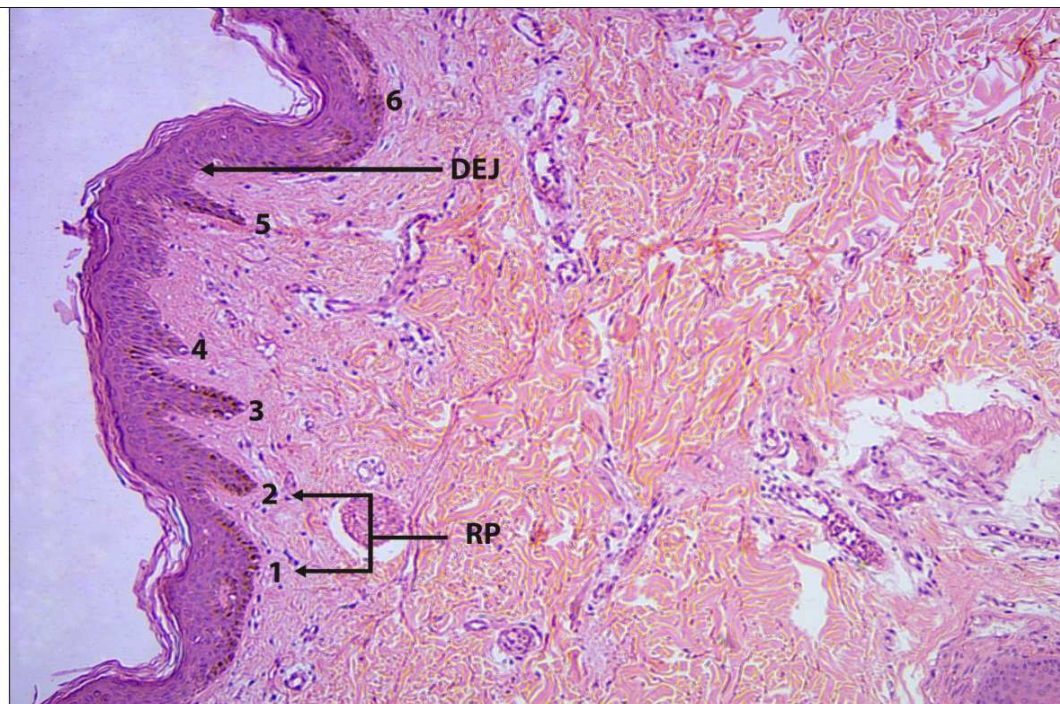


Figure 8 : Group B : 41- 50 Years (10x X 10)
RP : 6 Rete Pegs DEJ : Dermo - Epidermal Junction (Convolted)



Figure 9 : Group B : 41 - 50 Years (10x X 40)
DEJ : Dermo - Epidermal Junction (Convolted) E : Epidermis (Thick)

EPIDERMAL THICKNESS: GROUP C: 51-65Years

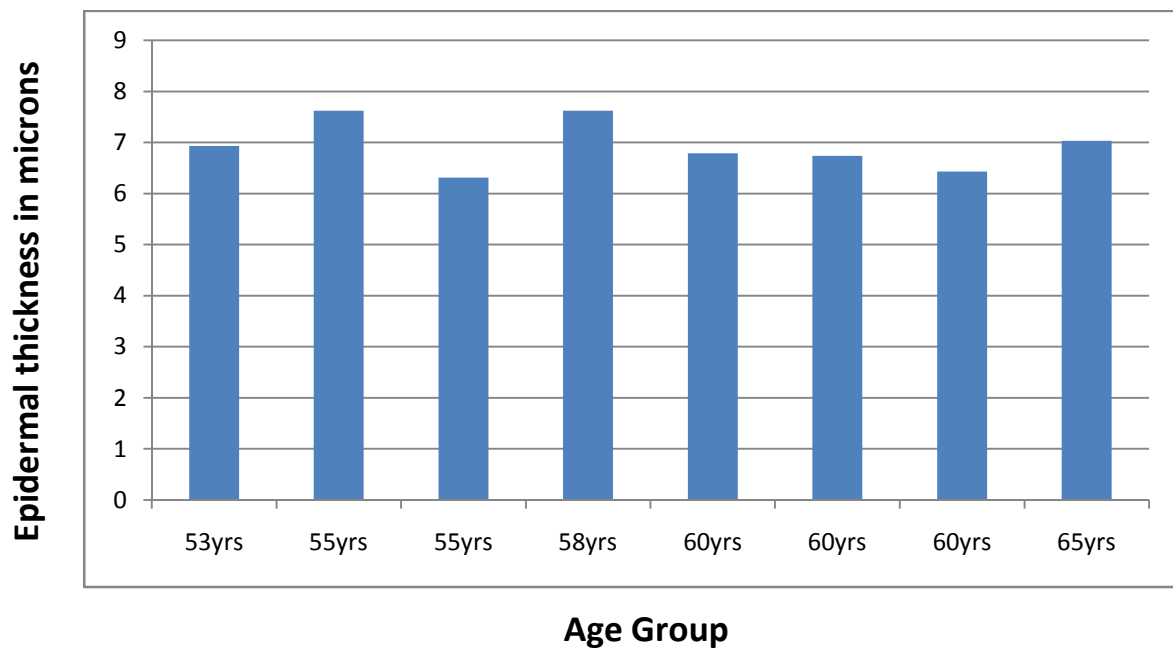
The epidermal thickness among Group C individuals from 51-65years of age was as found in Table 5. The mean thickness of the epidermis was 6.89micrometers.

Table: 5

AGE IN YEARS	EPIDERMAL THICKNESS IN MICROMETERS
53	6.93
55	7.62
55	6.31
58	7.62
60	6.79
60	6.74
60	6.43
65	7.03

The epidermal thickness in Group C persons from 51-65years of age is represented as bar diagram

Epidermal Thickness- Group C: 51-65 Years



RETE PEGS AND DERMO-EPIDERMAL JUNCTION: GROUP C

The average number of Rete Pegs was 5 to 6 as in Fig (10).

The depth of the Rete Pegs was reduced as in Fig (10) and Fig (11).

The Dermo-Epidermal junction was less convoluted compared to Group B individual.

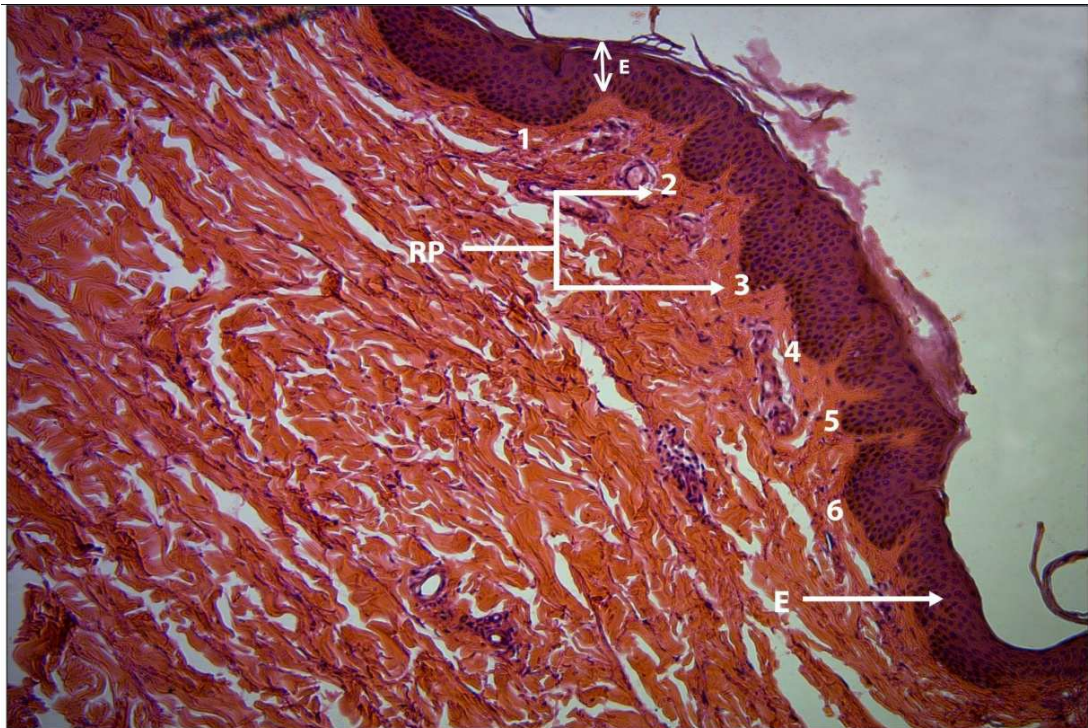


Figure 10 : Group C : 51 - 65 Years (10x X 10)
RP : 6 Rete Pegs (Reduced Depth) E : Epidermis (Thin)

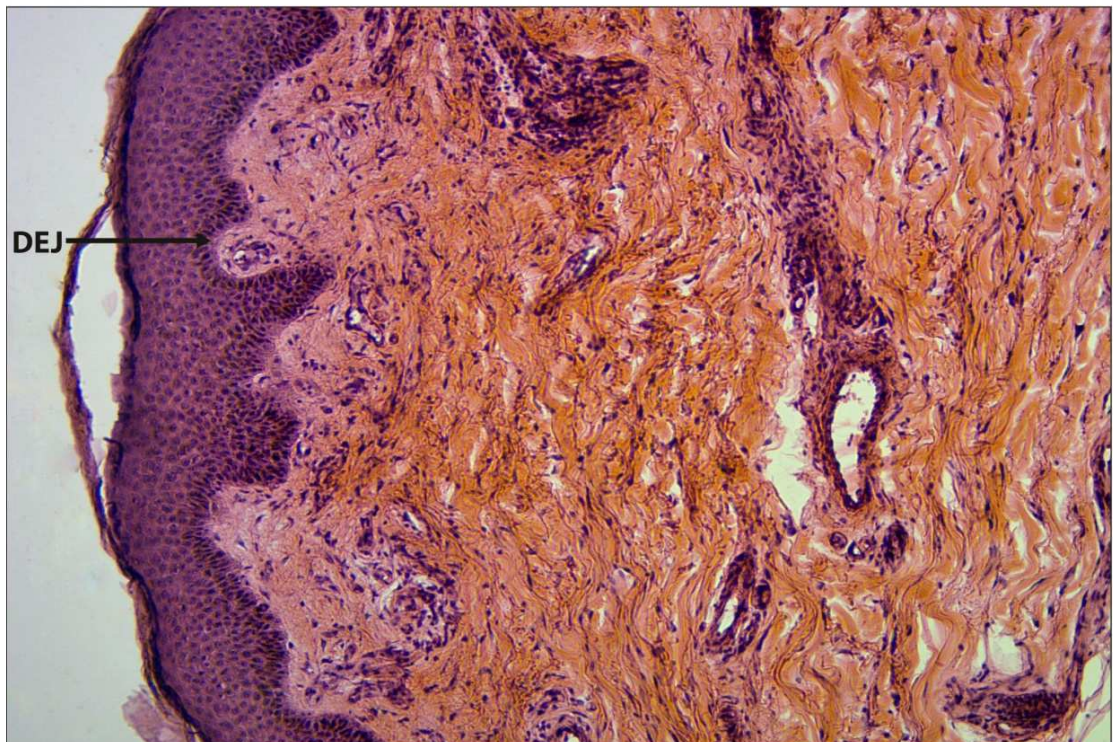


Figure 11 : Group C : 51 - 65 Years (10x X 10)
DEJ : Dermo - Epidermal Junction (Less Convolutd)

EPIDERMAL THICKNESS: GROUP D: > 65Years

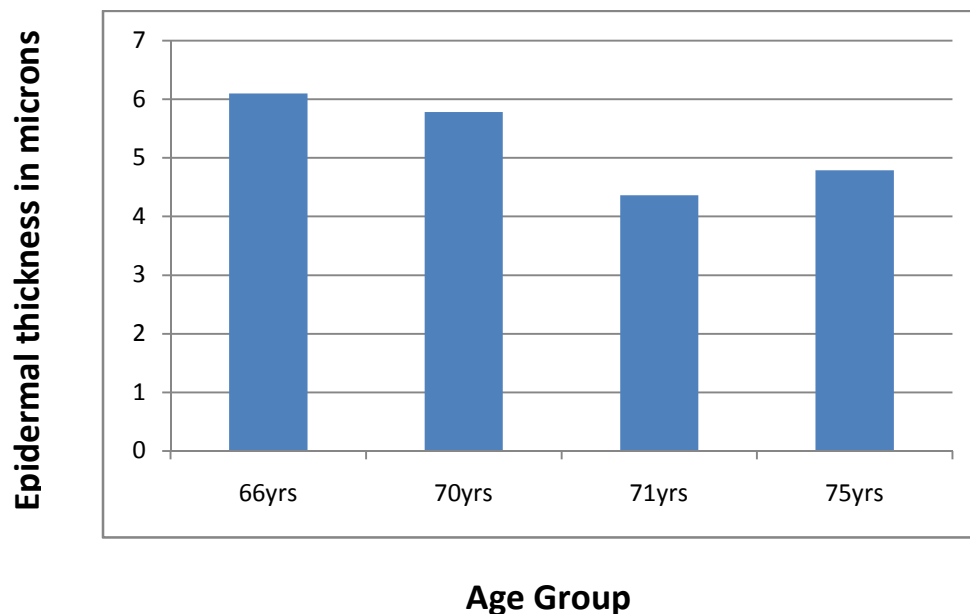
The epidermal thickness among Group D individuals of more than 65 years of age was as found in Table 6. The mean thickness of the epidermis was 5.25micrometers

Table: 6

AGE IN YEARS	THICKNESS OF THE EPIDERMIS IN MICROMETERS
66	6.10
70	5.78
71	4.363
75	4.79

The epidermal thickness in Group D persons of >65 years of age is represented as bar diagram.

Epidermal Thickness- Group D: > 65 Years



RETE PEGS AND DERMO-EPIDERMAL JUNCTION: GROUP D

The number of Rete Pegs was almost absent or only 1- 2 in number. The Dermo-Epidermal junction was almost flat as found in Fig (12) to Fig (15). The thickness was found to increase after 25 years of age and started to decrease from 50 years of age

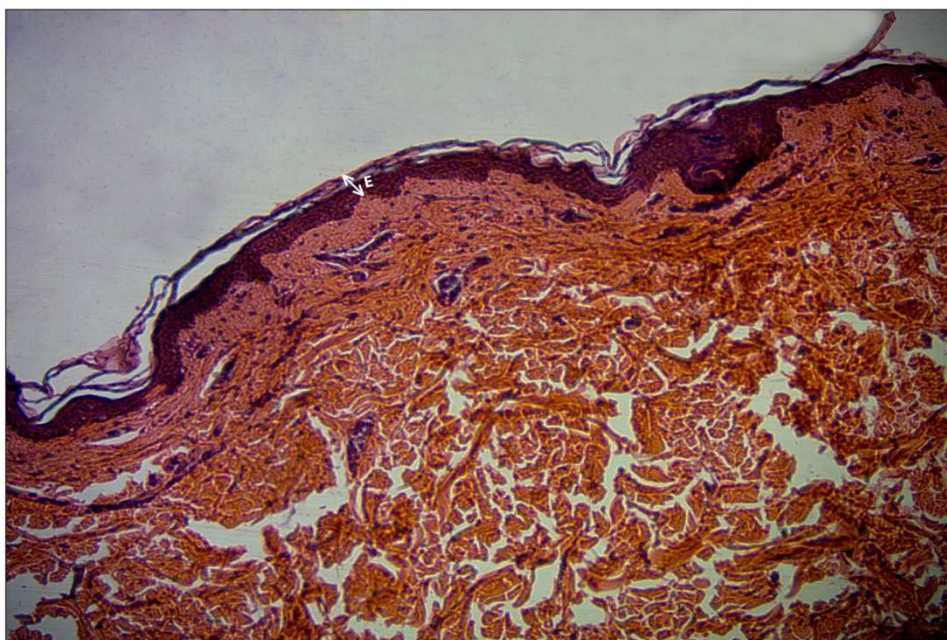


Figure 12 : Group D : > 65 Years (10x X 10)
E : Epidermis (Very thin)

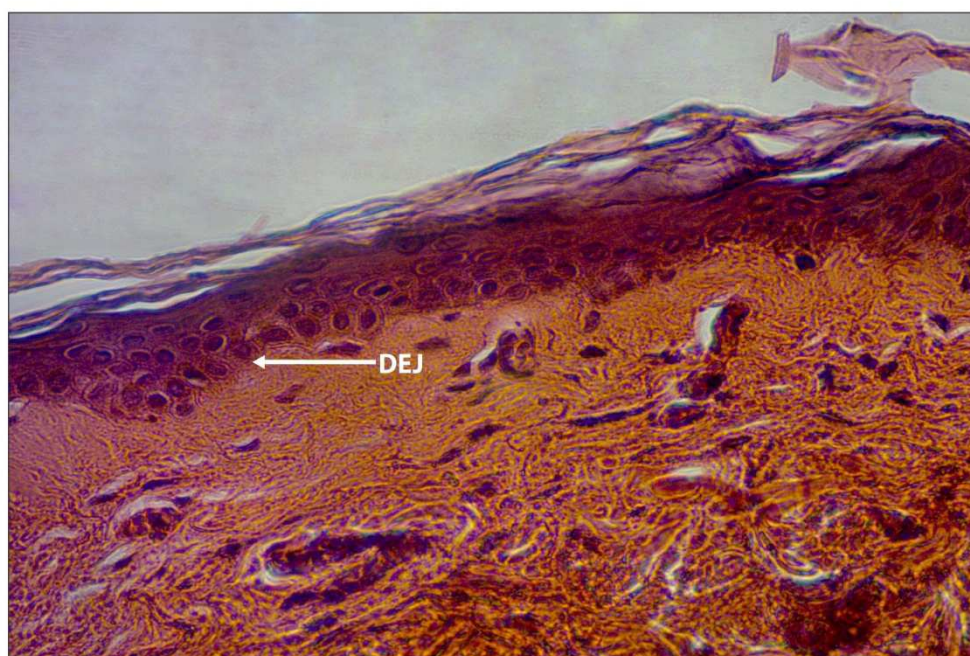


Figure 13 : Group D : > 65 Years (10x X 40)
DEJ : Dermo - Epidermal Junction (Flat)

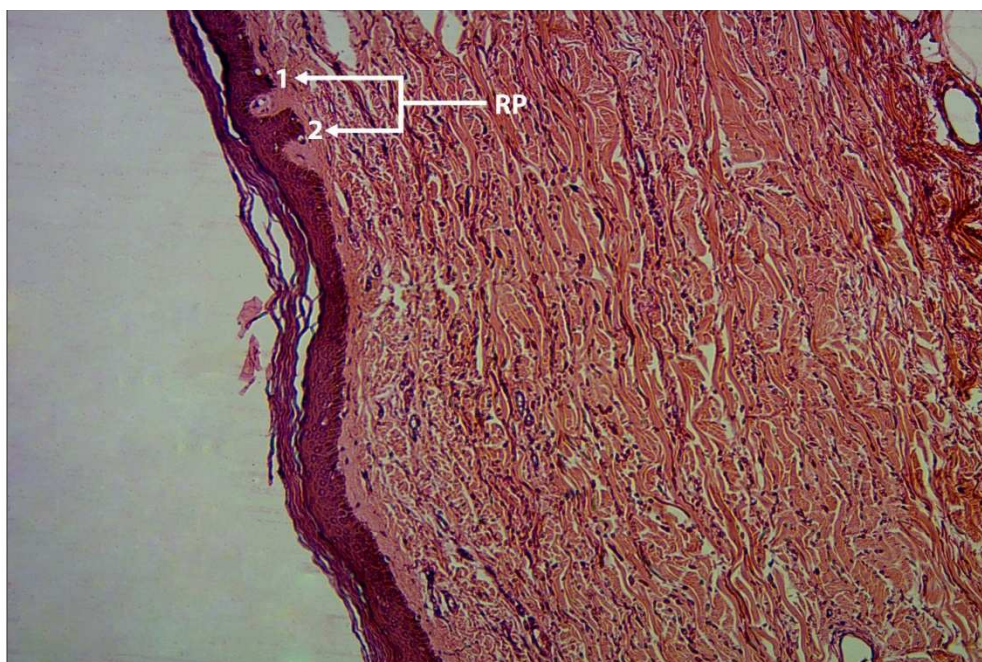


Figure 14 : Group D : > 65 Years (10x X 10)
RP : 2 Rete Pegs

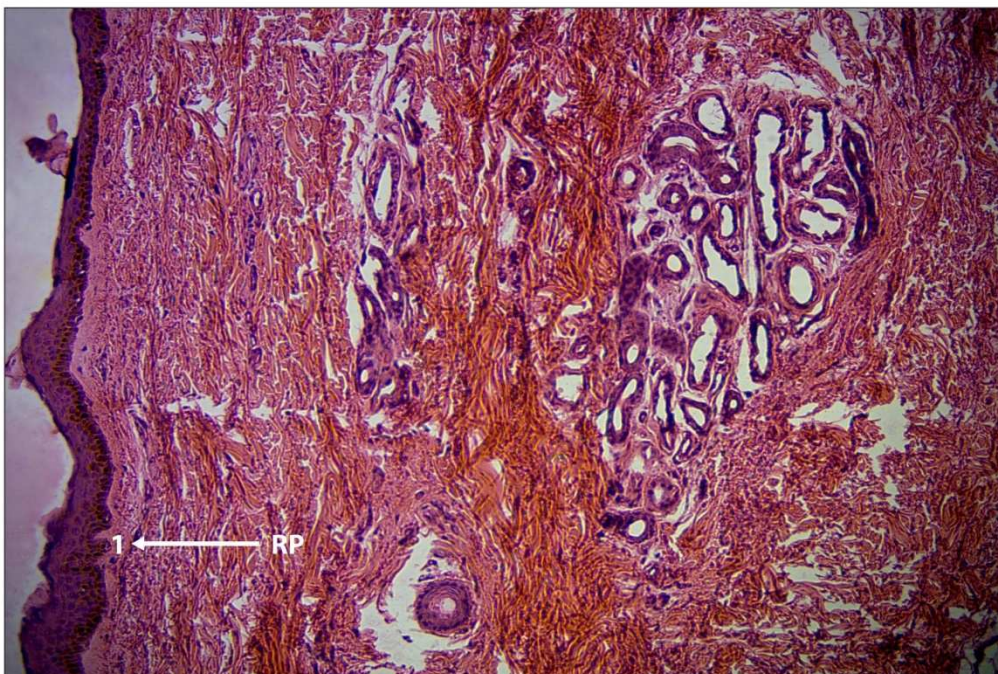


Figure 15 : Group D : > 65 Years (10x X 40)
RP : 1 Rete Peg

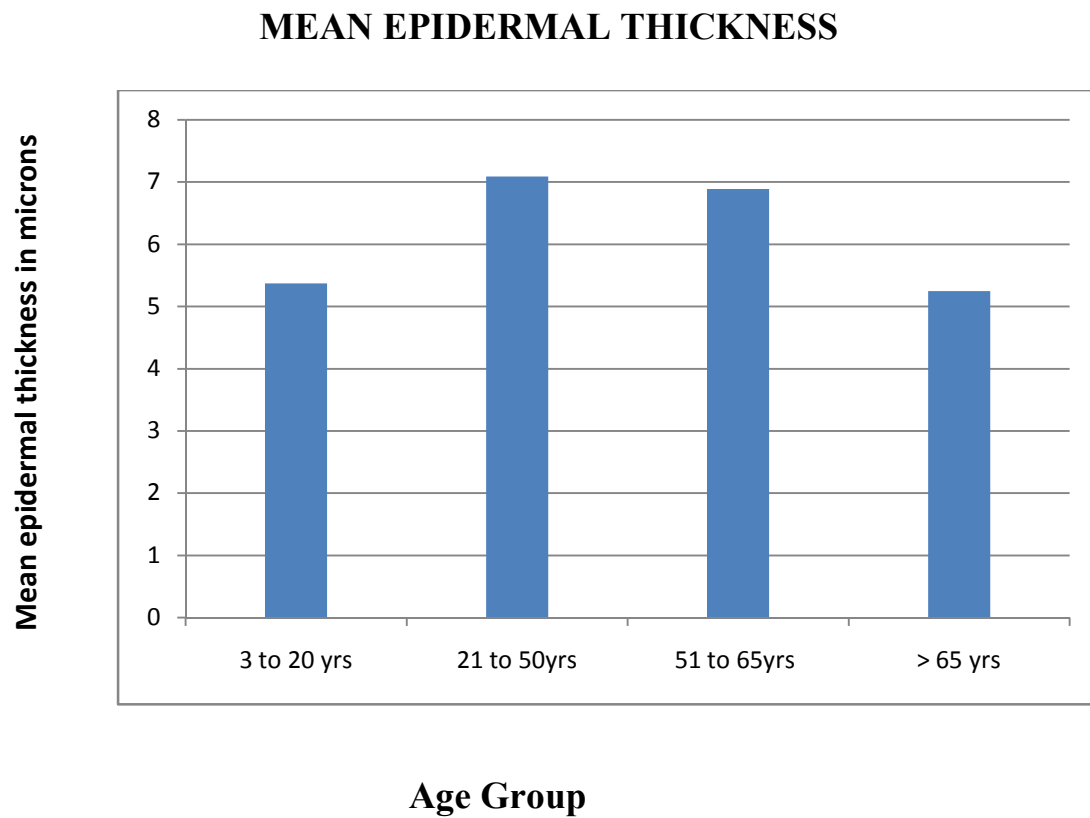
MEAN EPIDERMAL THICKNESS

The mean thickness of the epidermis among Group A persons of 3-20years of age, Group B persons of 21-50years of age, Group C persons of 51-65years of age and Group D persons of more than 65years of age was as found in Table 7.

Table: 7

AGE GROUP IN YEARS	MEAN EPIDERMAL THICKNESS IN MICROMETERS
A 3-20	5.37
B 21-50	7.09
C 51-65	6.89
D >65	5.25

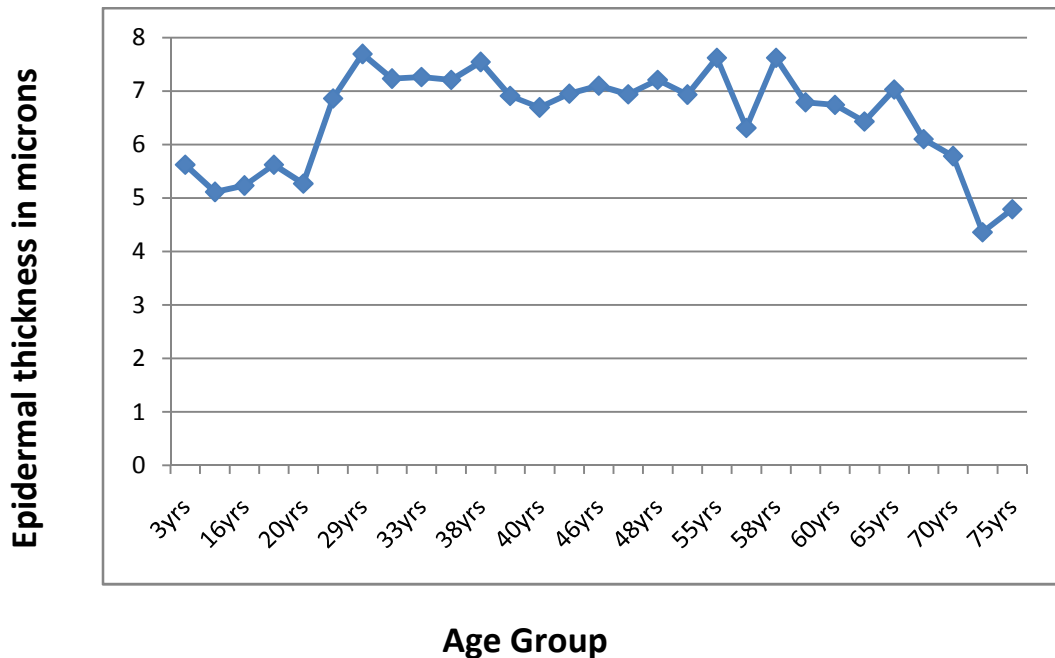
The mean thickness of the epidermis in Group A (3-20yrs), Group B (21-50yrs), Group C (51-65yrs) and Group D (>65yrs) is represented as bar diagram.



EPIDERMAL THICKNESS AMOUNG 3-75yrs OF AGE

The difference in the thickness of the epidermis from 3 years to 75 years of age was varying. The epidermis in Group A persons from 3-20years of age is thin. The thickness of the epidermis started to increase from 21 years of age and the epidermis is thick in Group B persons of 21- 50 years of age. The thickness of the epidermis starts to decrease from 51years of age and the epidermis is thin in Group C persons from 51-65 years of age. The epidermis in very thin in Group D persons of > 65 years of age as represented in the line diagram.

Epidermal thickness from 3-75 years of age



RETE PEGS

The difference in the number of Rete Pegs among Group A persons from 3-20years, Group B persons from 21-50 years, Group C persons from 51-65years and Group D persons > 65 years of age was tabulated in Table 8.

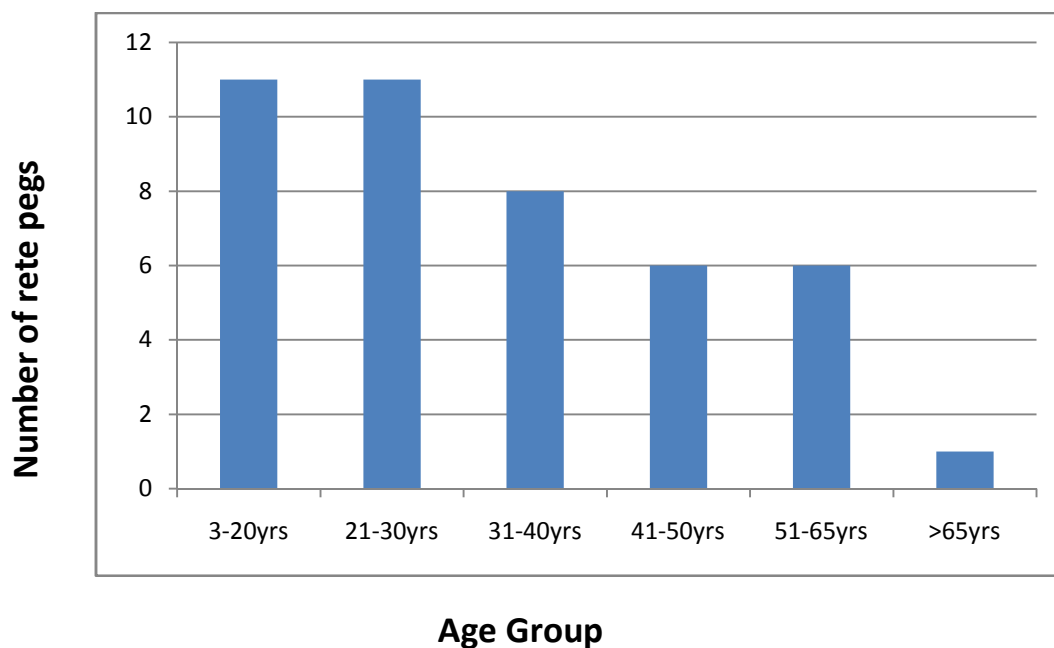
Table: 8 - Rete Pegs

AGE GROUP (in years)	NUMBER OF RETE PEGS	FIGURE NUMBER
3 -20	11	Fig (1)
21 – 30	11	Fig (4)
31 – 40	8	Fig (6)
41 – 50	6	Fig (8)
51 - 65	6	Fig (10)
>65	1	Fig (14)

The number of Rete Pegs was found to increase in Group A persons of 3-21years and in Group B persons from 21-30years.

The number was found to get reduced in Group B persons from 31years of age with marked decrease in Group C persons of 51-65 Years of age. In Group D persons of more than 65 years the number of Rete Pegs was almost absent or only one or two in number as represented in the bar diagram.

Rete Pegs: 3- 75 years of age



Statistical analysis was done to compare the variations in the thickness of the epidermis among four age groups using ANOVA and tabulated in Table 9.

Table: 9 - ANOVA

AGE GROUP IN YEARS	NUMBER OF PERSONS IN EACH GROUP	MEAN	STANDARD DEVIATION	F VALUE	P VALUE
3-20	5	5.3700	.23569	32.831	<0.001
21-50	12	7.1325	.28603		
51-65	8	6.9338	.48583		
>65	4	5.2575	.81790		
TOTAL	29	6.5152	.91896		

The difference in the thickness of the epidermis between group A from 3 years to 20 years of age and Group B from 21 years to 50 years of age was found to be statistically significant with P value < 0.001.

The difference in epidermal thickness between Group A from 3 years to 20 years of age and Group C from 51 years to 65 years of age was found to be statistically significant with P value < 0.001.

The difference in epidermal thickness between Group B from 21 years to 50 years of age and Group D of more than 65 years of age was found to be statistically significant with P value of < 0.001 .

The difference in epidermal thickness between Group C from 51 years to 65 years of age and Group D of more than 65 years of age was found to be statistically significant with P value of < 0.001 .

The difference in epidermal thickness between Group A from 3 years to 20 years of age and Group D of more than 65 years of age was not statistically significant.

SKIN APPENDAGES

SWEAT GLANDS

GROUP A:

In **3-20 years of age** the skin specimens showed minimal number of sweat glands as in Fig (16) and Fig (17).

GROUP B:

In **21-30 years of age**, the number of sweat glands was less as in group A as found in Fig (18).

In **31-40 years of age**, the sweat glands were found to be increased in number than 21-30 years age group as found in Fig (19) and Fig (20).

In **41-50 years of age**, the sweat glands were found to be increased in number similar to 31-40years age grouped individuals as in Fig (21).

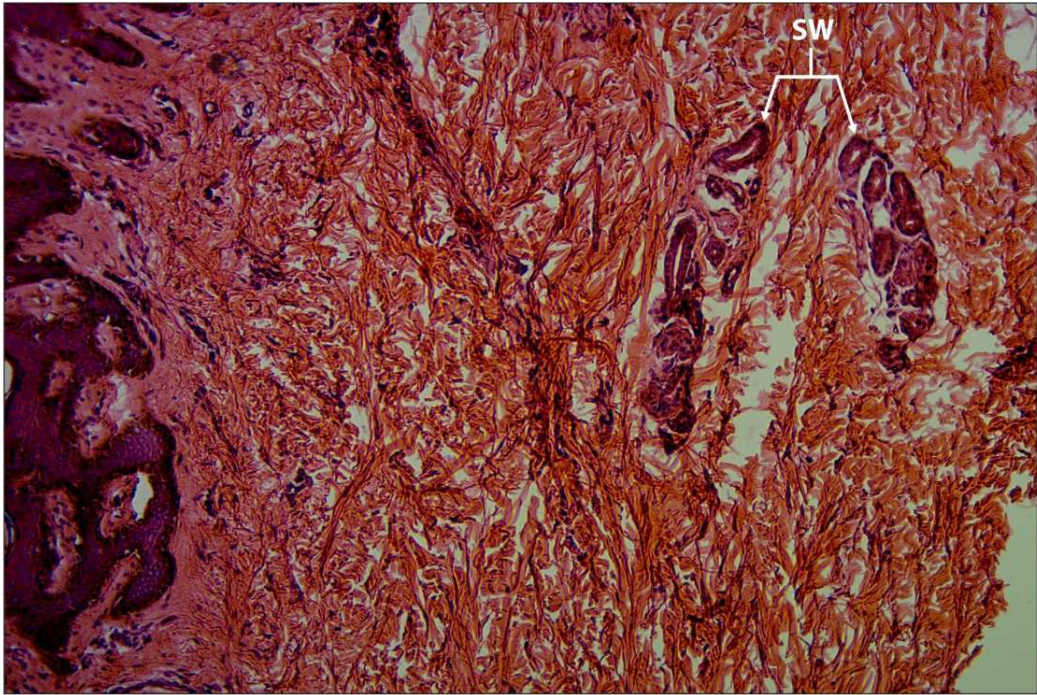


Figure 16 : Group A : 3 - 20 Years (10x X 10)
SW : Sweat Glands (Decreased Number)

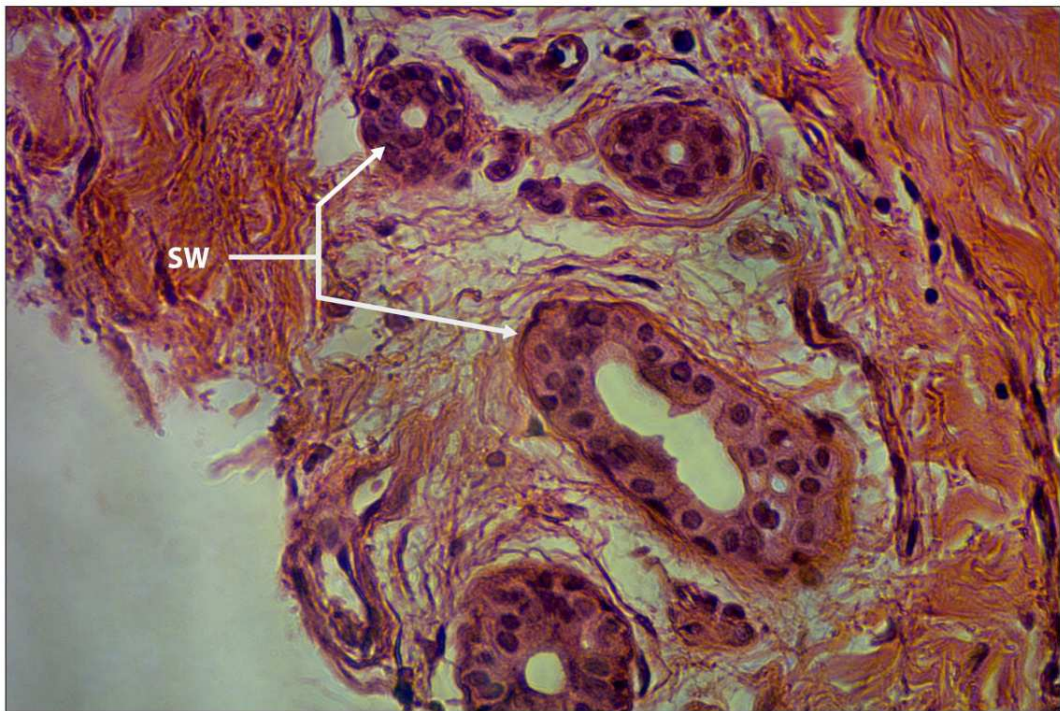


Figure 17 : Group A : 3 - 20 Years (10x X 40)
SW : Sweat Glands (Decreased Number)

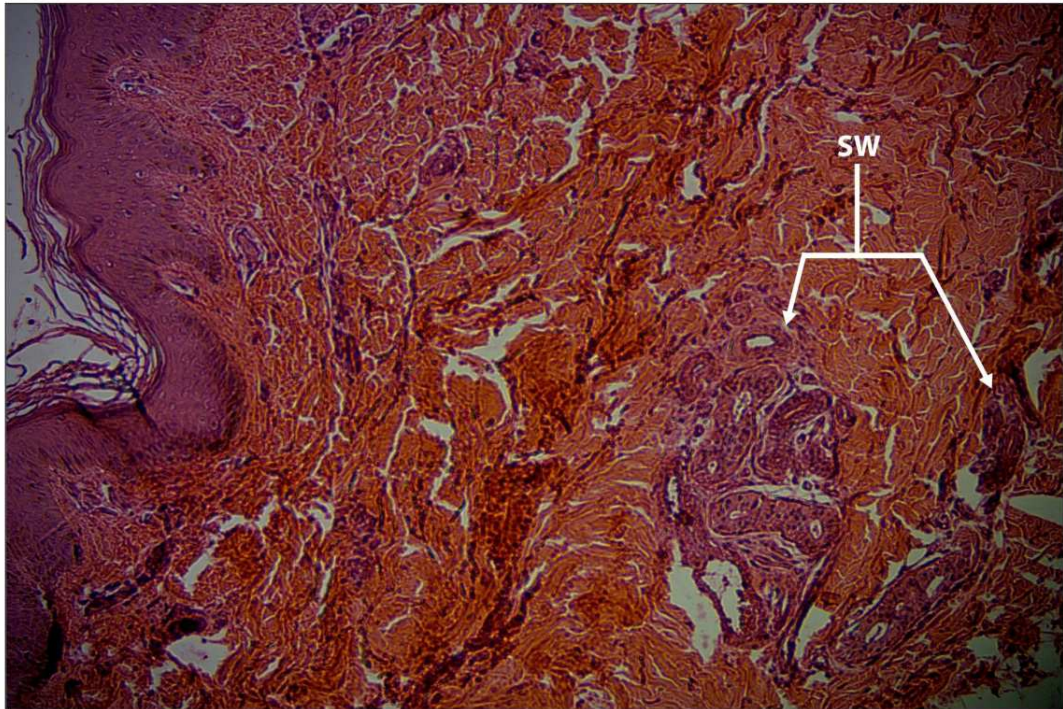


Figure 18 : Group B : 21 - 30 Years (10x X 10)
SW : Sweat Glands (Decreased Number)

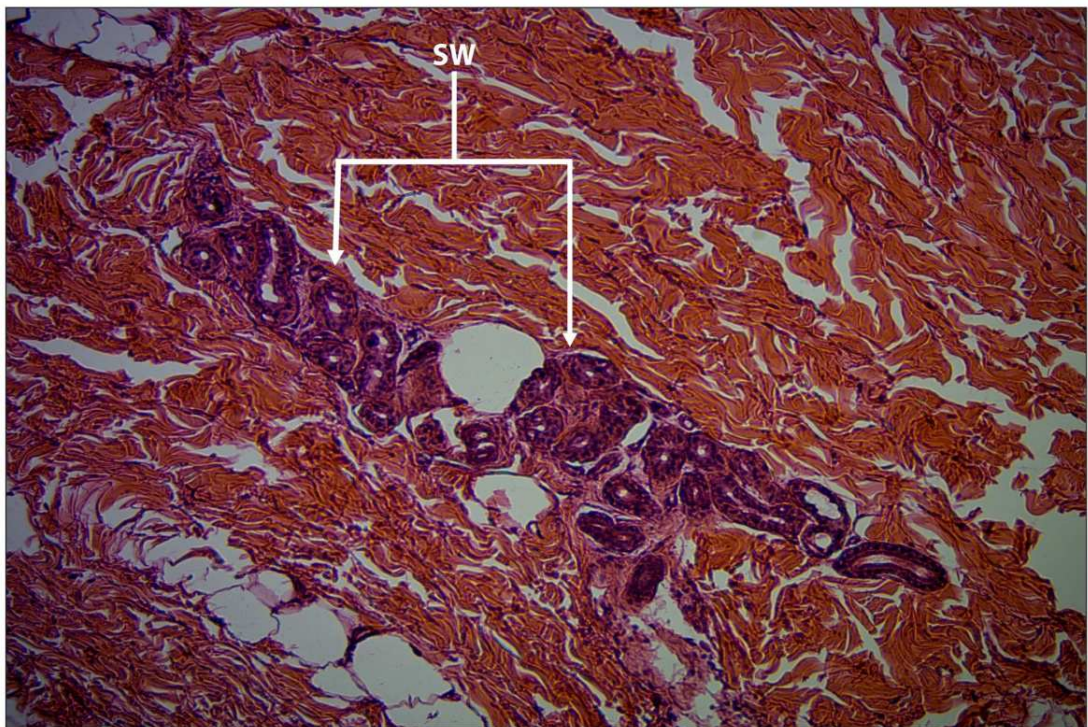


Figure 19 : Group B : 31 - 40 Years (10x X 10)
SW : Sweat Glands (Increased Number)

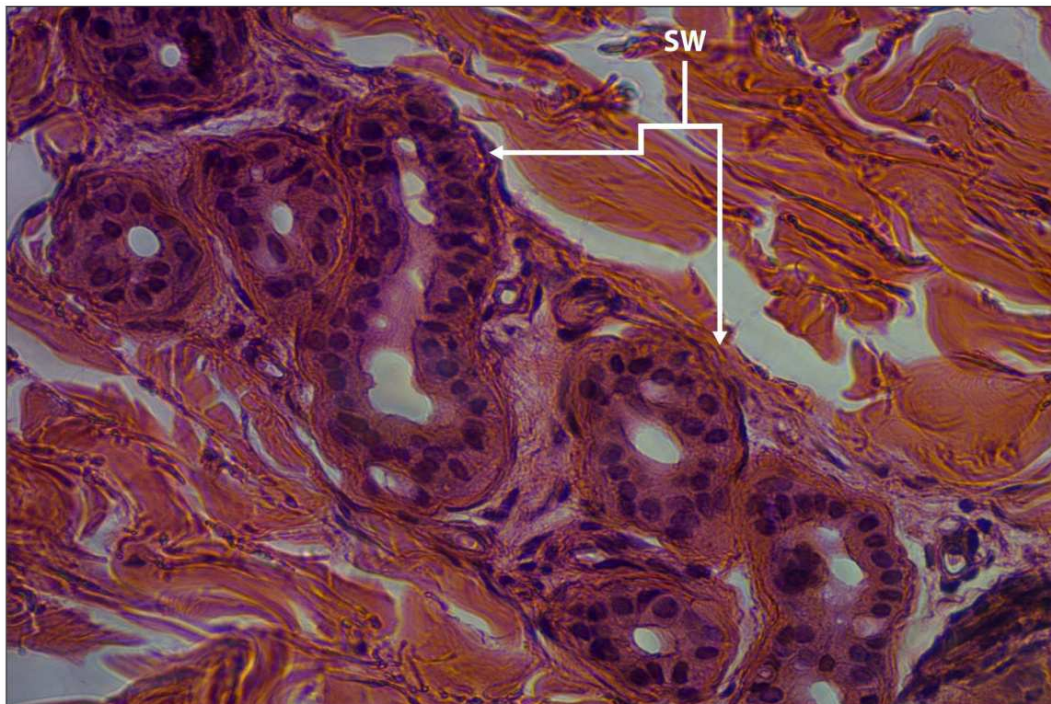


Figure 20 : Group B : 31 - 40 Years (10x X 40)
SW : Sweat Glands (Increased Number)

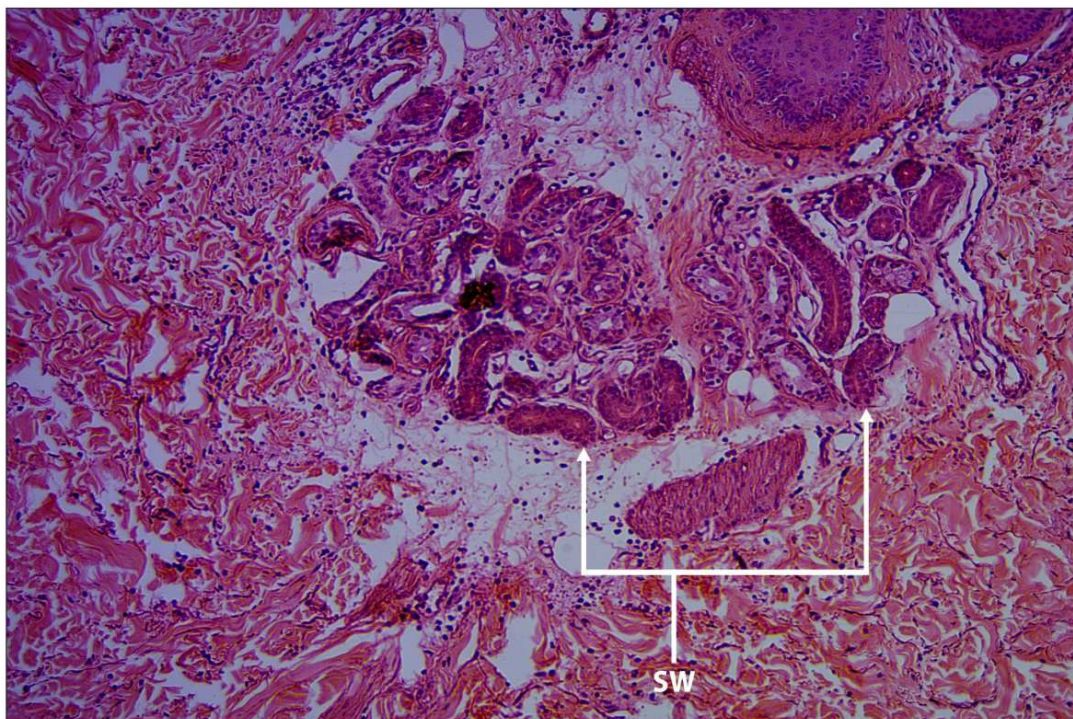


Figure 21 : Group B : 41 - 50 Years (10x X 10)
SW : Sweat Glands (Increased Number)

GROUP C:

In **51-60 years of age** number of sweat glands was found to be almost similar to Group B as found in fig (22).

GROUP D:

In Skin specimens of **> 65 years of age**, the number of sweat glands was found to be less than Group C individuals as found in Fig (23), (24) and (25).

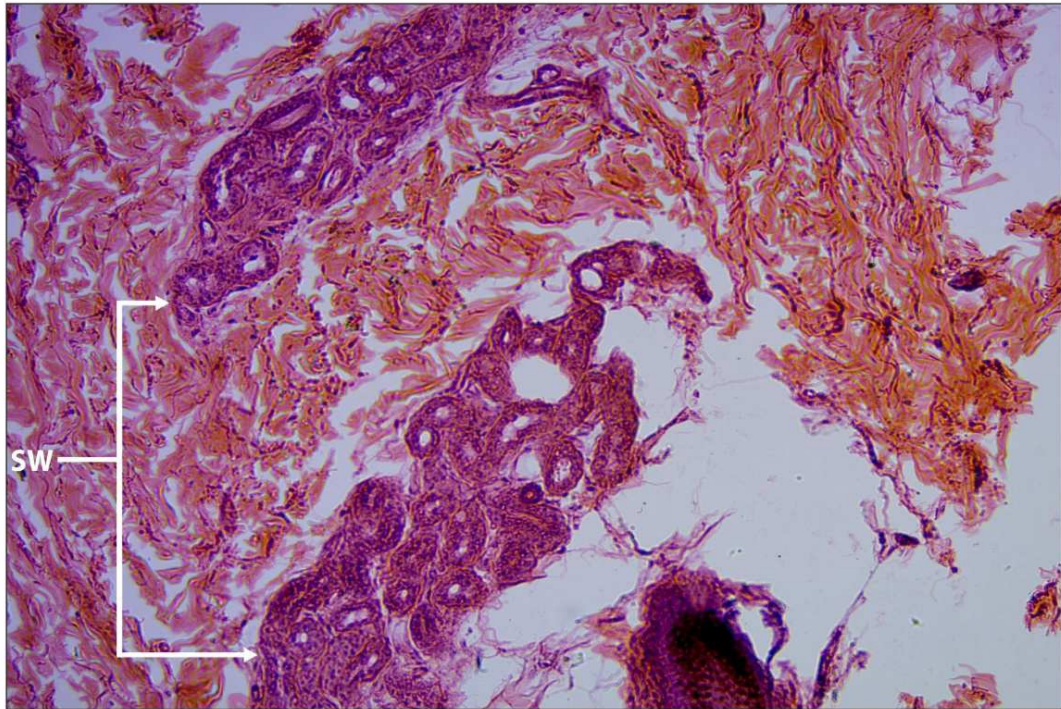


Figure 22 : Group C : 51 - 65 Years (10x X 10)
SW : Sweat Glands (Increased Number)

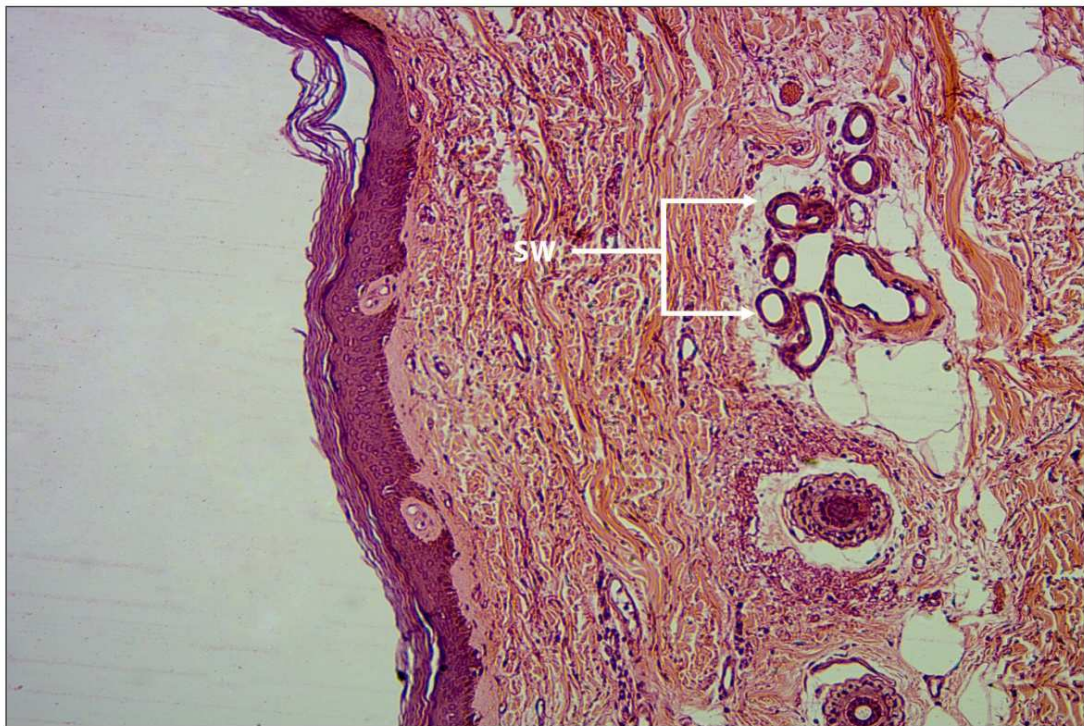


Figure 23 : Group D : > 65 Years (10x X 10)
SW : Sweat Glands (Decreased Number)

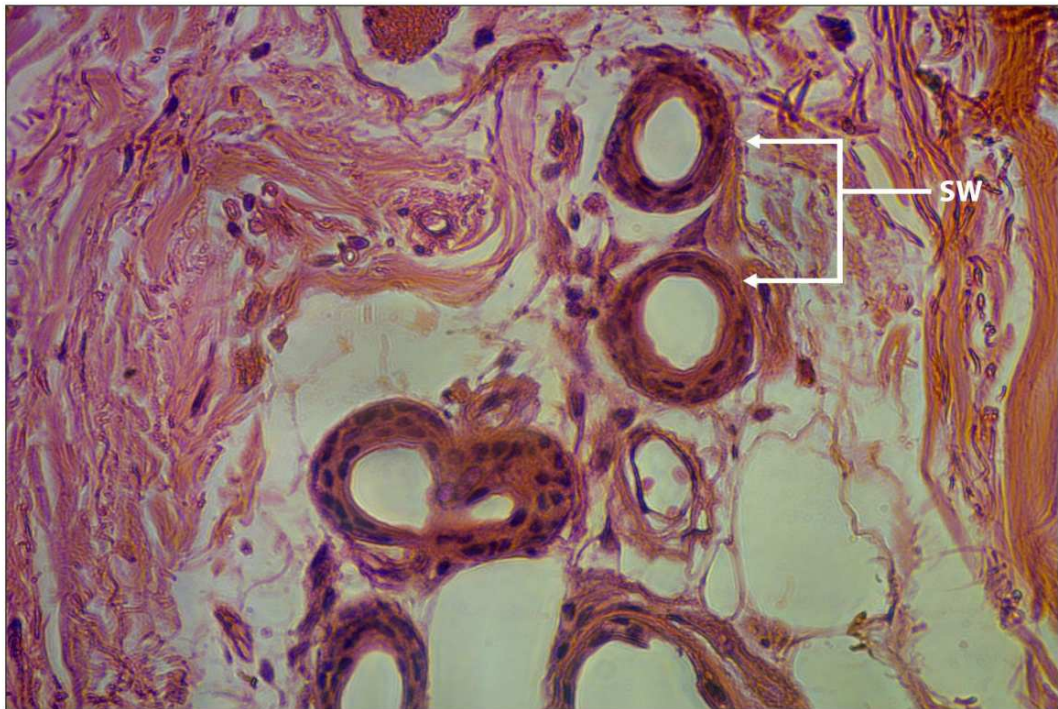


Figure 24 : Group D : > 65 Years (10x X 40)
SW : Sweat Glands (Decreased Number)

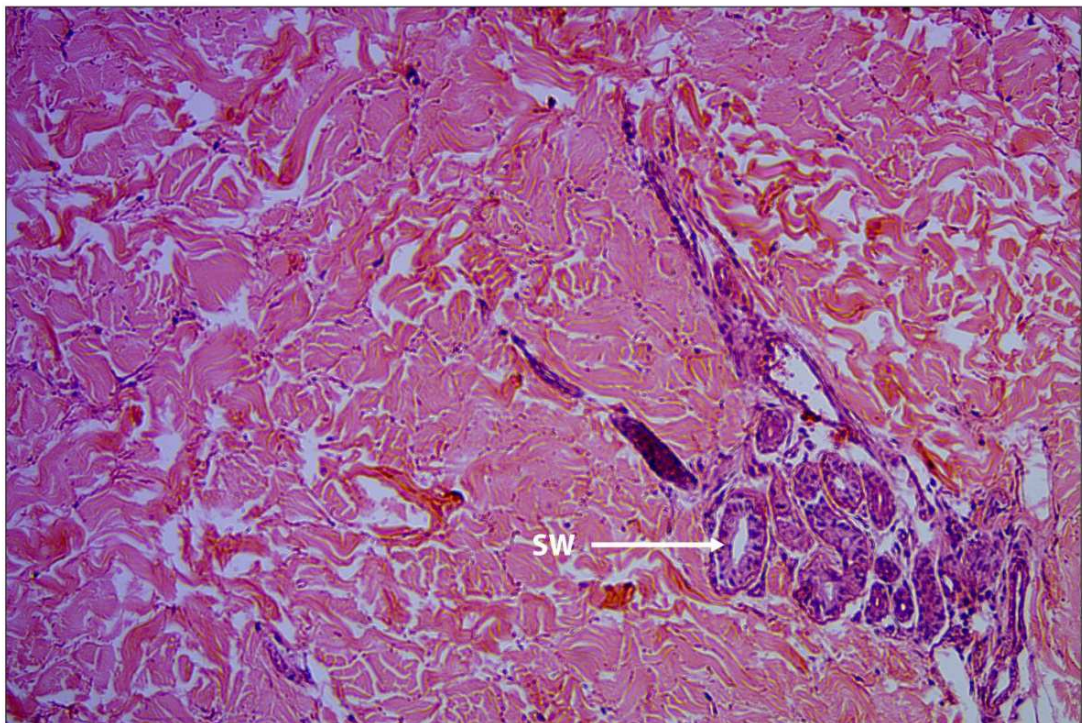


Figure 25 : Group D : > 65 Years (10x X 10)
SW : Sweat Glands (Decreased Number)

SEBACEOUS GLANDS

The sebaceous glands were found to have no significant variation in the size and the number with increasing age, but a significant difference was noted at different sites of the body.

The size and the number of sebaceous glands was found to be less in the abdomen and chest region as found in Fig (26) and Fig (27).

The size was found to be less in the leg and thigh region as in Fig (28) and Fig (29).

More number of sebaceous glands was noted in the face in the forehead Fig (30) and Fig (31).

The sebaceous glands were highly branched in the cheek Fig (32).

The duct of the sebaceous glands was found to be opening into the root of the hair follicle and the Arrector pili muscle was present at the base of the sebaceous gland as found in Fig (33) and Fig (34).

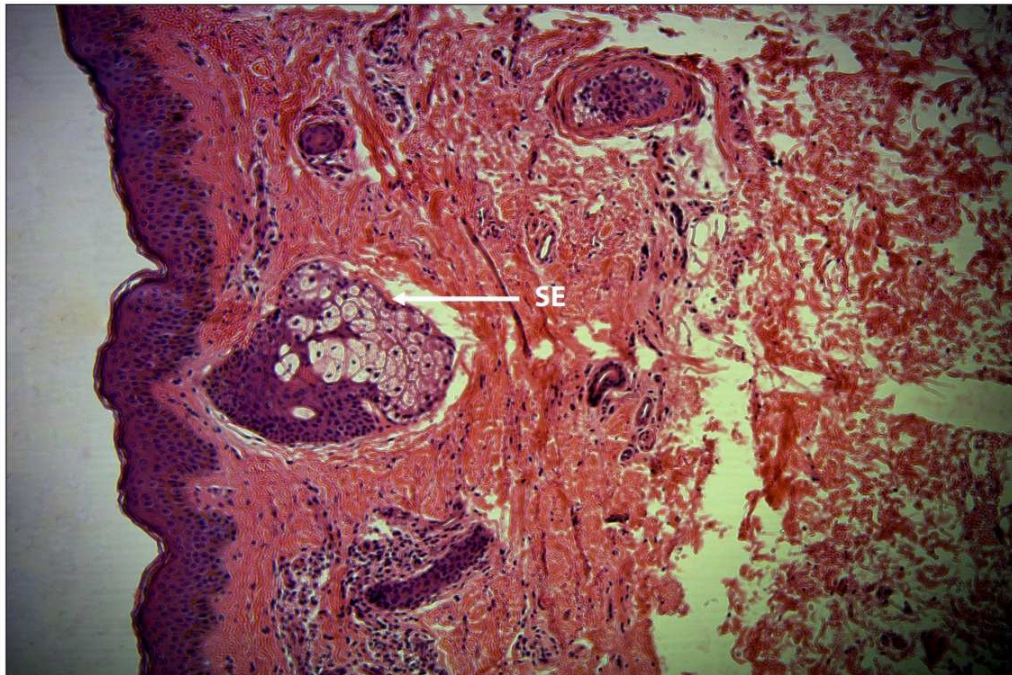


Figure 26 : Skin Specimen - Abdomen Region (10x X 10)
SE : Sebaceous Glands (Decreased Number and Size)

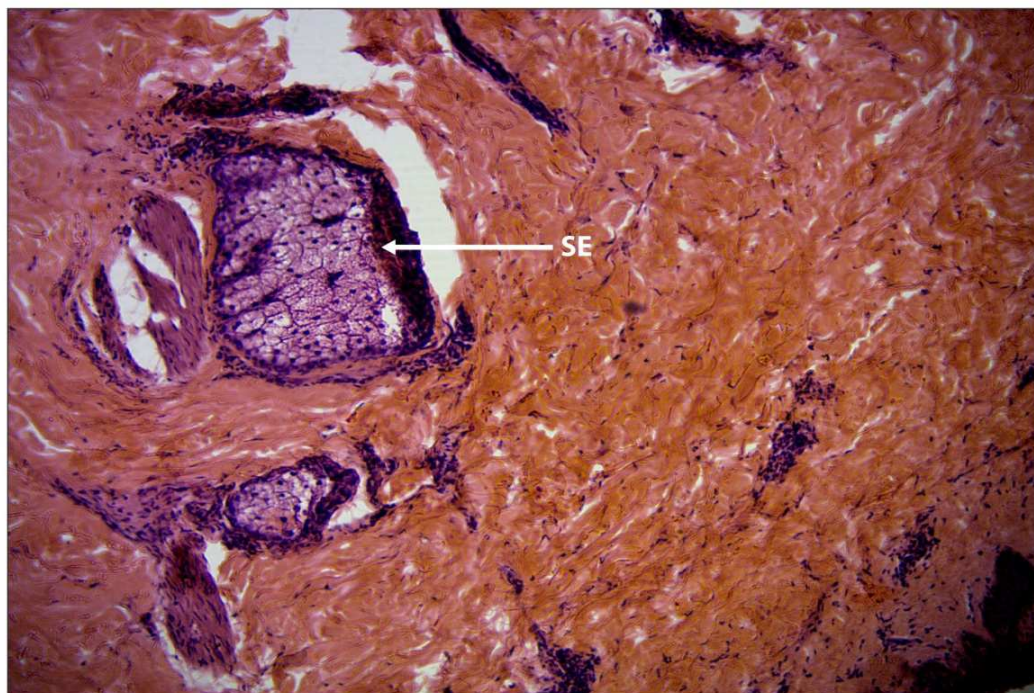


Figure 27 : Skin Specimen - Chest Region (10x X 10)
SE : Sebaceous Glands (Decreased Number and Size)

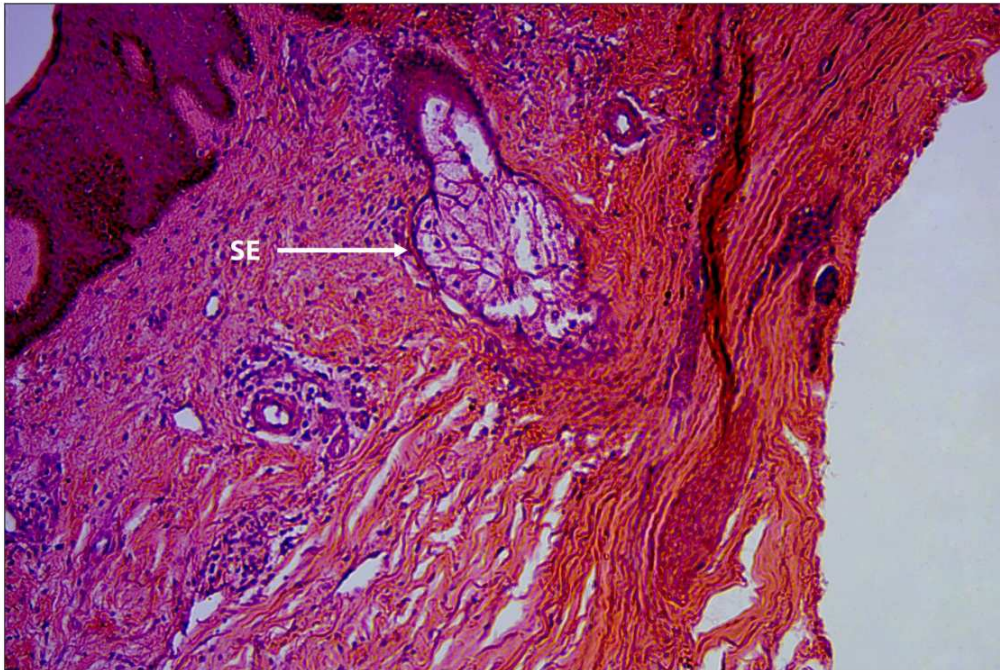


Figure 28 : Skin Specimen - Leg Region (10x X 10)
SE : Sebaceous Glands (Decreased Number and Size)

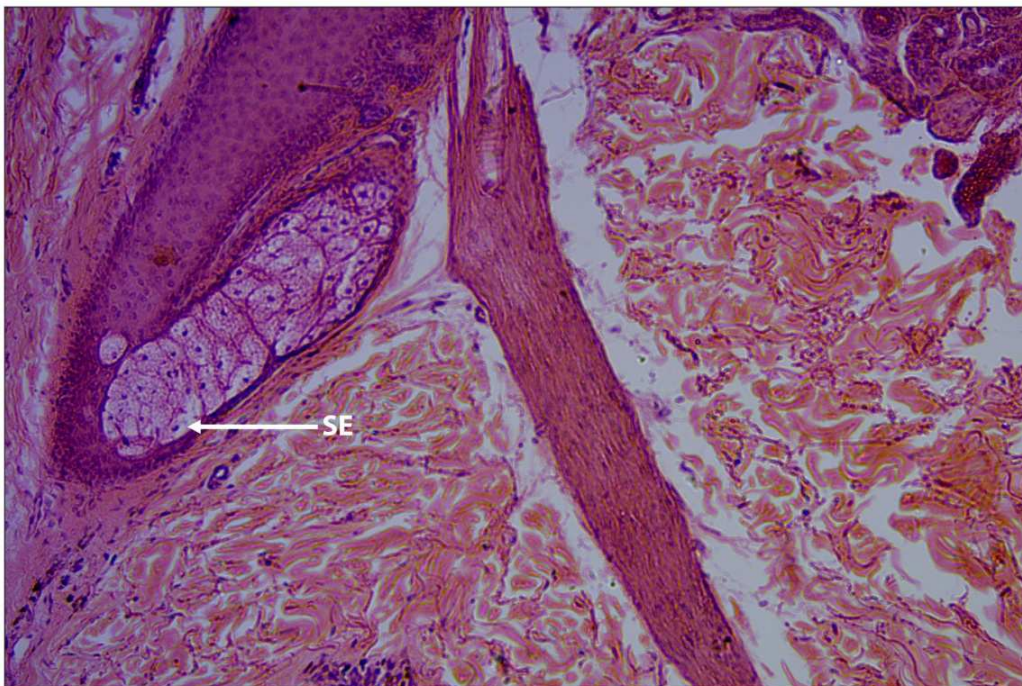


Figure 29 : Skin Specimen - Thigh Region (10x X 10)
SE : Sebaceous Glands (Decreased Number and Size)

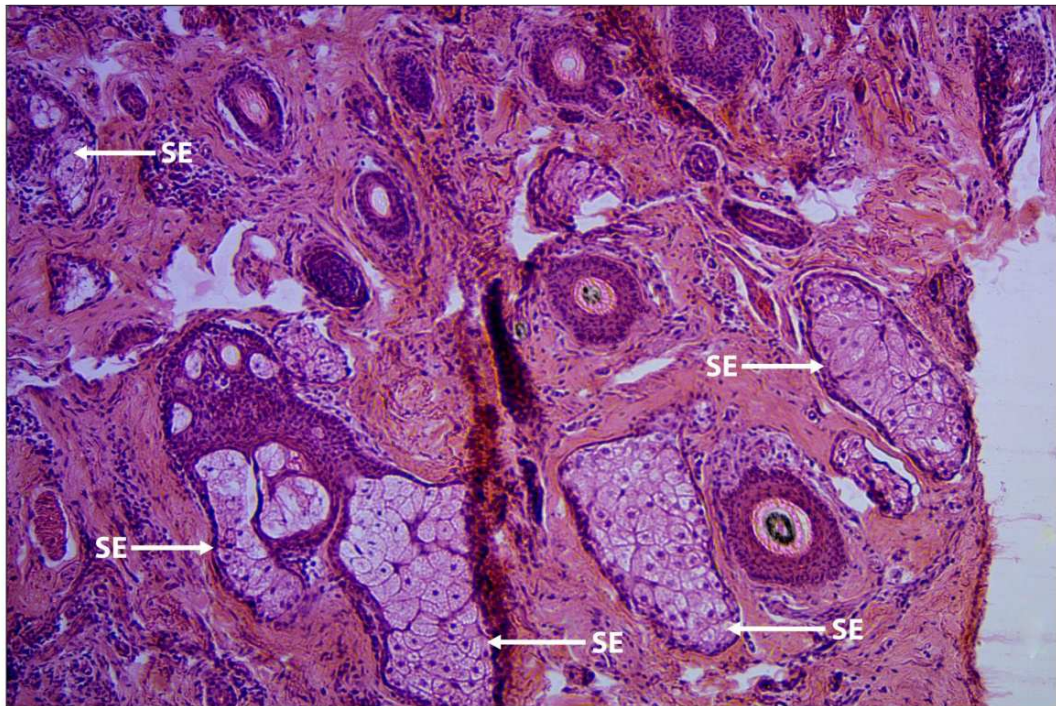


Figure 30 : Skin Specimen - Forehead (10x X 10)
SE : Sebaceous Glands (Increased Number)

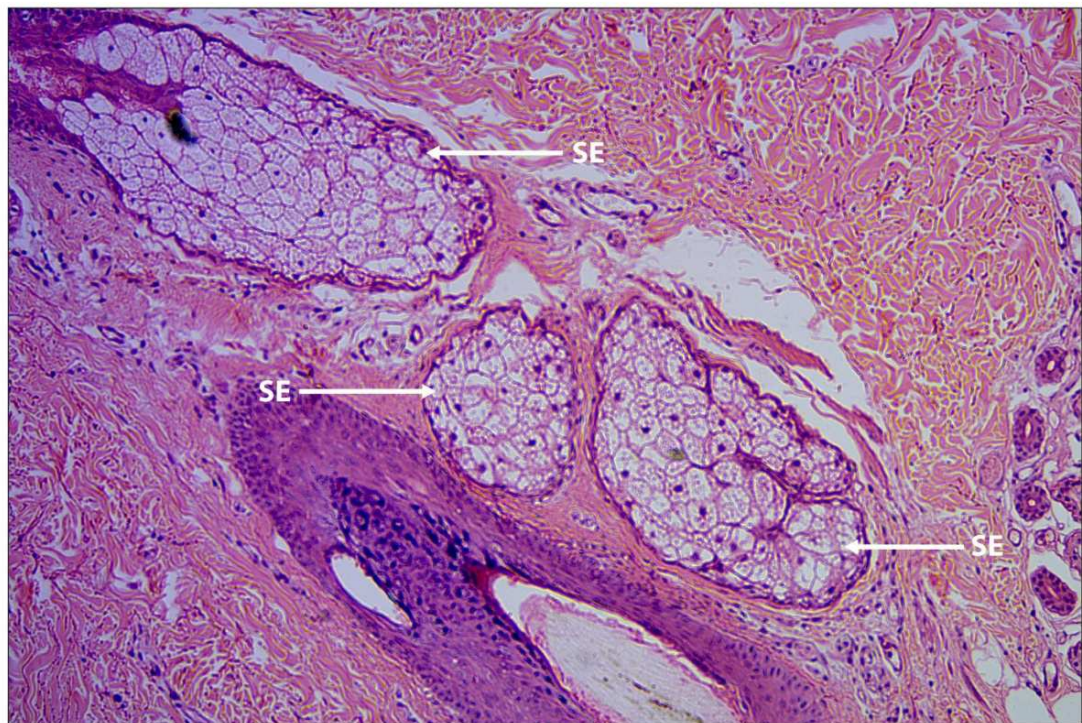


Figure 31 : Skin Specimen - Forehead (10x X 10)
SE : Sebaceous Glands (Increased Number and Size)

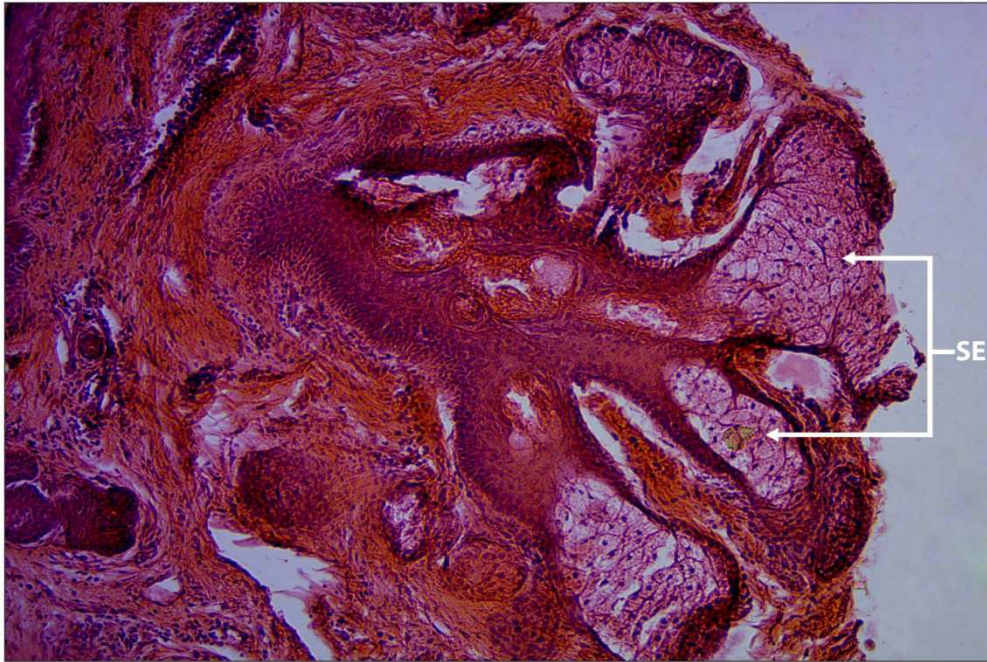


Figure 32 : Skin Specimen - Cheek (10x X 10)
SE : Sebaceous Glands (Highly Branched)

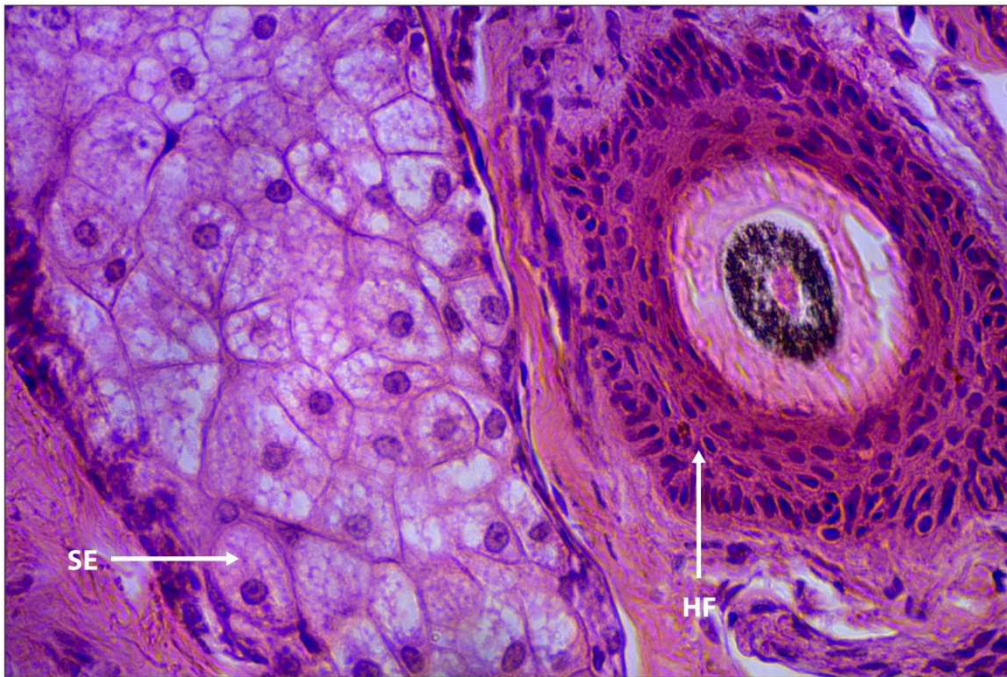


Figure 33 : Hair Follicle with Sebaceous Gland (10x X 40)
SE : Sebaceous Gland HF : Hair Follicle

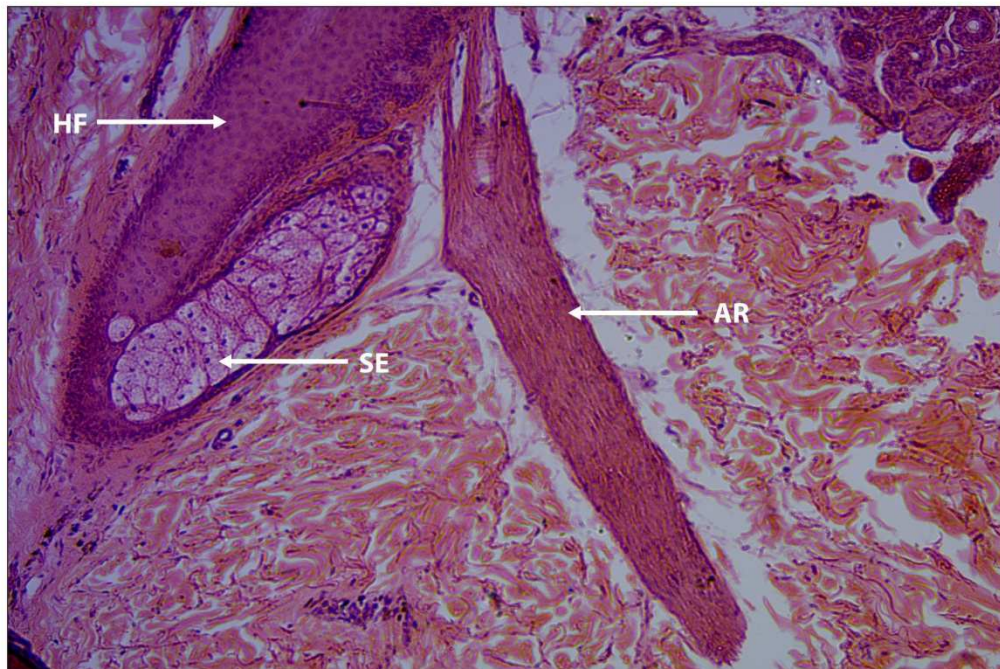


Figure 34 : Hair Follicle with Sebaceous Gland with Arrector Pili Muscle (10x X 10)
SE : Sebaceous Gland HF : Hair Follicle AR : Arrector Pili Muscle

DERMIS:

Verhoeff Van Gieson stain was done to study the changes in the elastic fibers with increasing age.

The changes in the collagen fibers were also noted.

The fibers in black color are the elastic fibers and the fibers in pink color are the collagen fibers,

GROUP A:

In this age group from **3 years to 20 years of age**, the section of the skin showed increased quantity of elastic and collagen fibers. Both the fibers were compactly arranged in dermis and were found to be thick and elongated as found in Fig (35), (36) and fig (37).

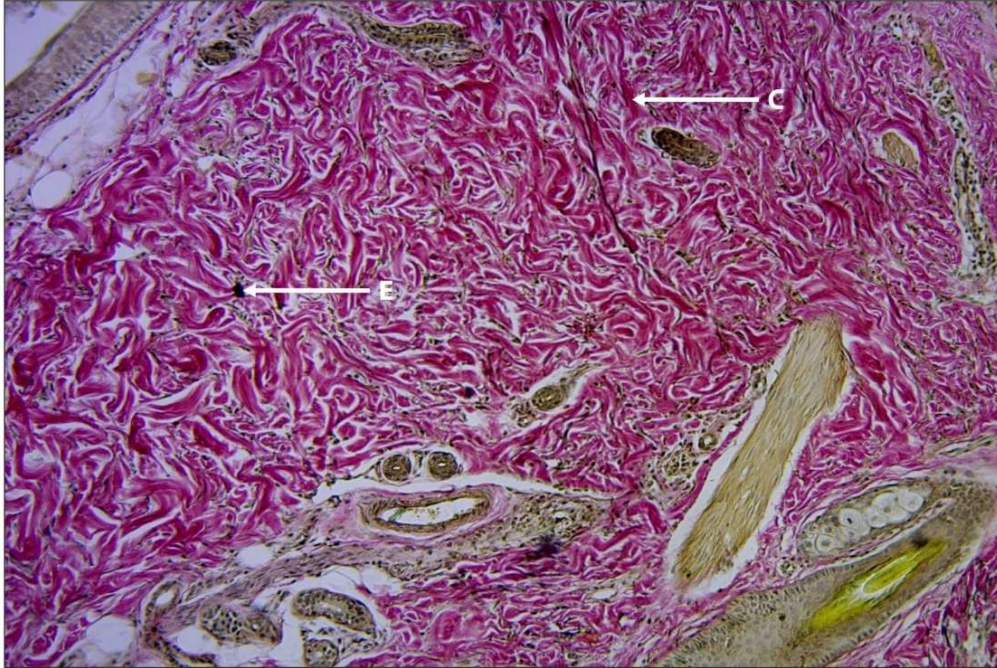


Figure 35 : Verhoeff Van Geison Stain Group A : 3 - 20 Years (10x X 10)
E : Elastic Fibers(Black) C : Collagen Fibers (Pink)

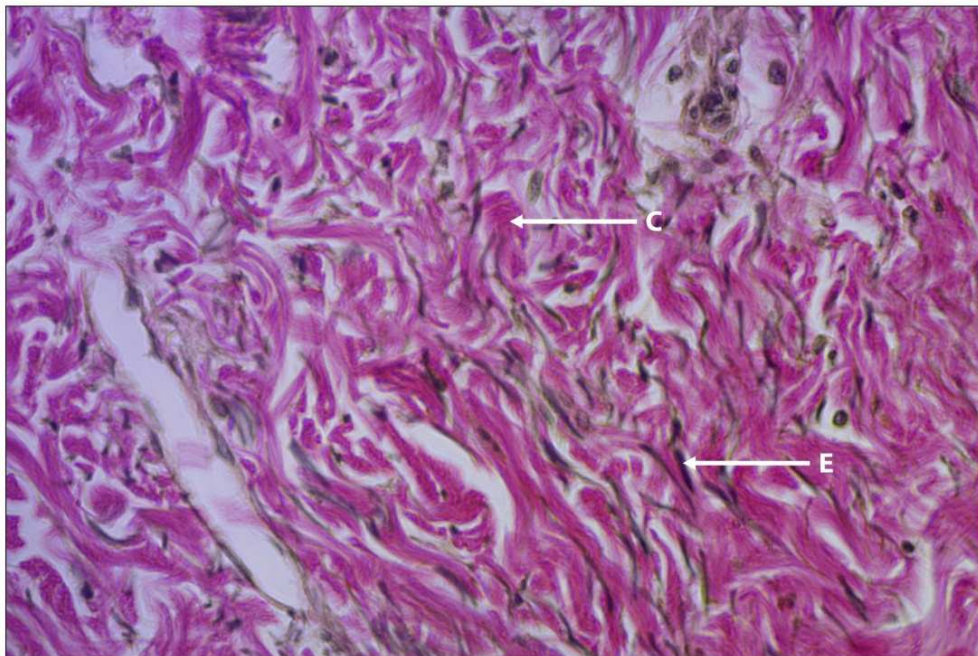


Figure 36 : Verhoeff Van Geison Stain Group A : 3 - 20 Years (10x X 40)
E : Elastic Fibers (Black) (Thick and Elongated) C : Collagen Fibers (Pink)(Thick and Elongated)

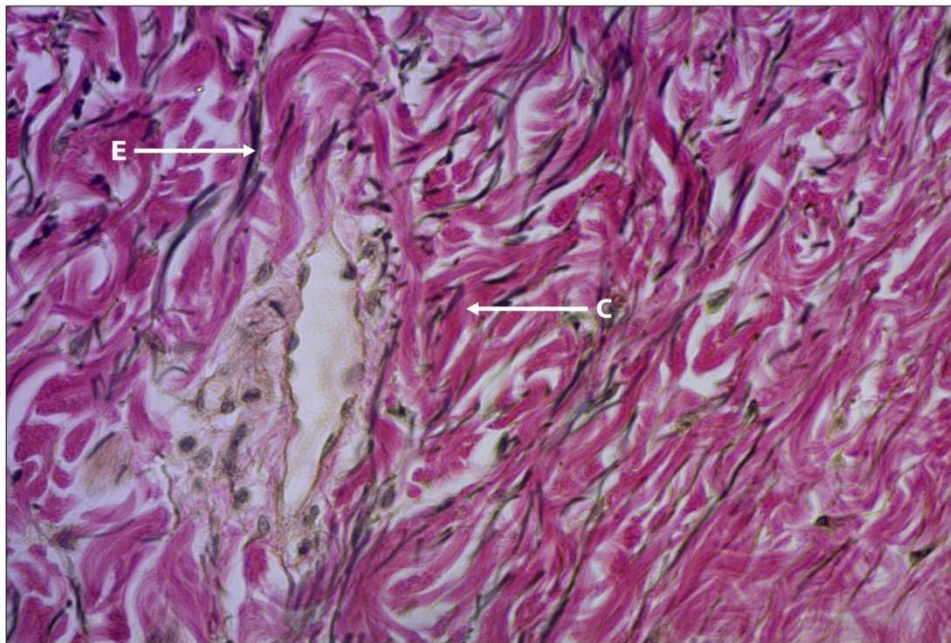


Figure 37 : Verhoeff Van Geison Stain Group A : 3 - 20 Years (10x X 40)

E : Elastic Fibers (Black) (Increased number, Thick and Elongated)

C : Collagen Fibers (Pink)(Increased number, Thick and Elongated)

GROUP B:

21-30years:

The skin specimens from this age group were found to have more number of elastic fibers which were found to be more elongated and thick as found in Fig (38), Fig (39) and Fig (40), similar to the appearance as in group A individuals between 3-20years of age.

The collagen fibers were more thick and elongated in dermis as found in Fig (41).

31-40years:

In skin specimen in this age group also showed more number of collagen fibers and elastic fibers similar to Group B and they were observed to be thick and elongated as found in Fig (42), (43) and (44).

These findings were similar to the observations as in 21-30 years age group.

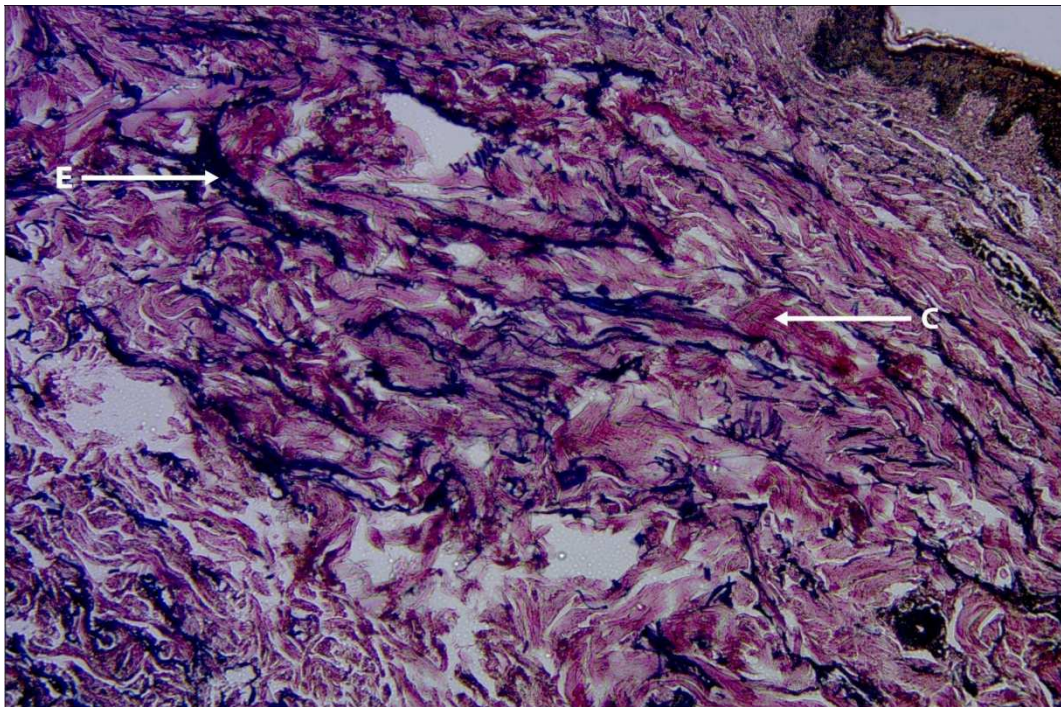


Figure 38 : Verhoeff Van Geison Stain Group B : 21 - 30 Years (10x X 10)

E : Elastic Fibers (Black) (Increased number, Thick and Elongated)

C : Collagen Fibers (Pink) (Increased number, Thick and Elongated)

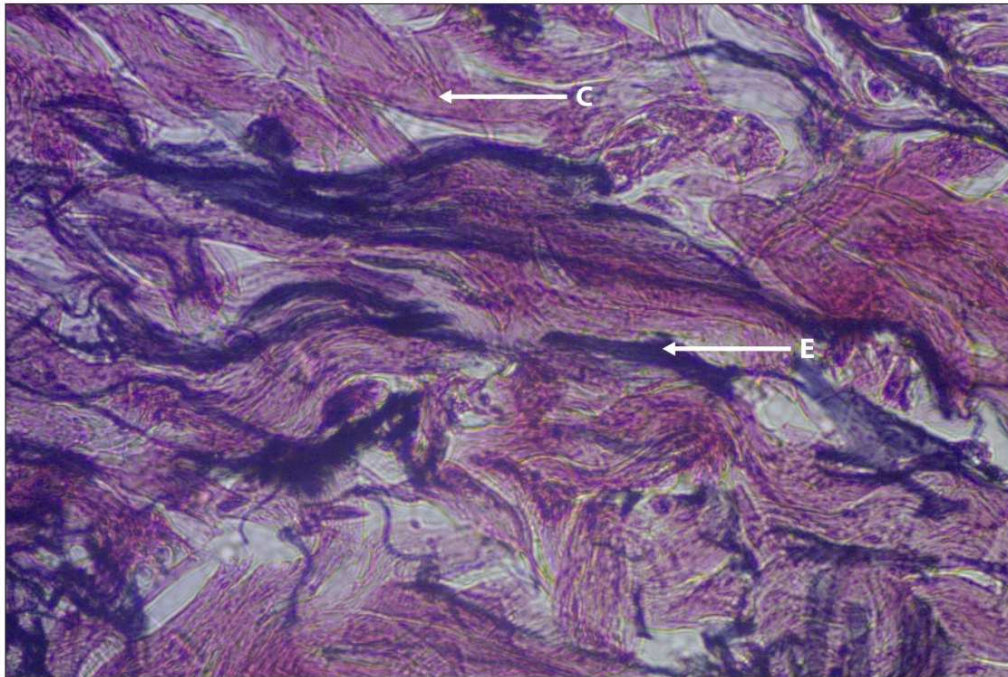


Figure 39 : Verhoeff Van Geison Stain Group B : 21 - 30 Years (10x X 40)

E : Elastic Fibers (Black) (Increased number, Thick and Elongated)

C : Collagen Fibers (Pink)(Increased number, Thick and Elongated)

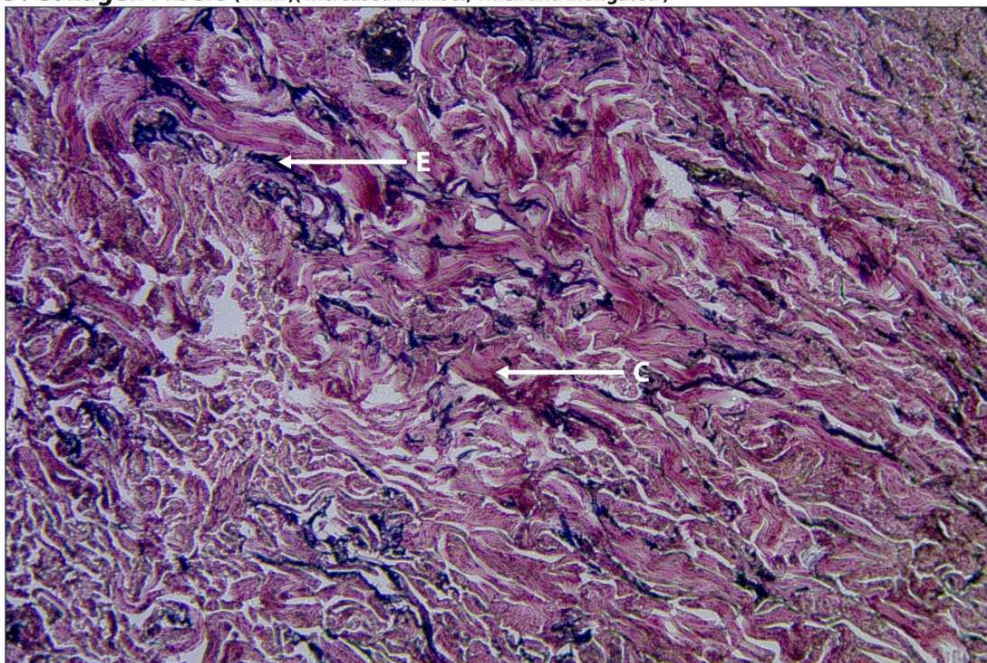


Figure 40 : Verhoeff Van Geison Stain Group B : 21 - 30 Years (10x X 10)

E : Elastic Fibers (Black) (Increased number, Thick and Elongated)

C : Collagen Fibers (Pink)(Increased number, Thick and Elongated)

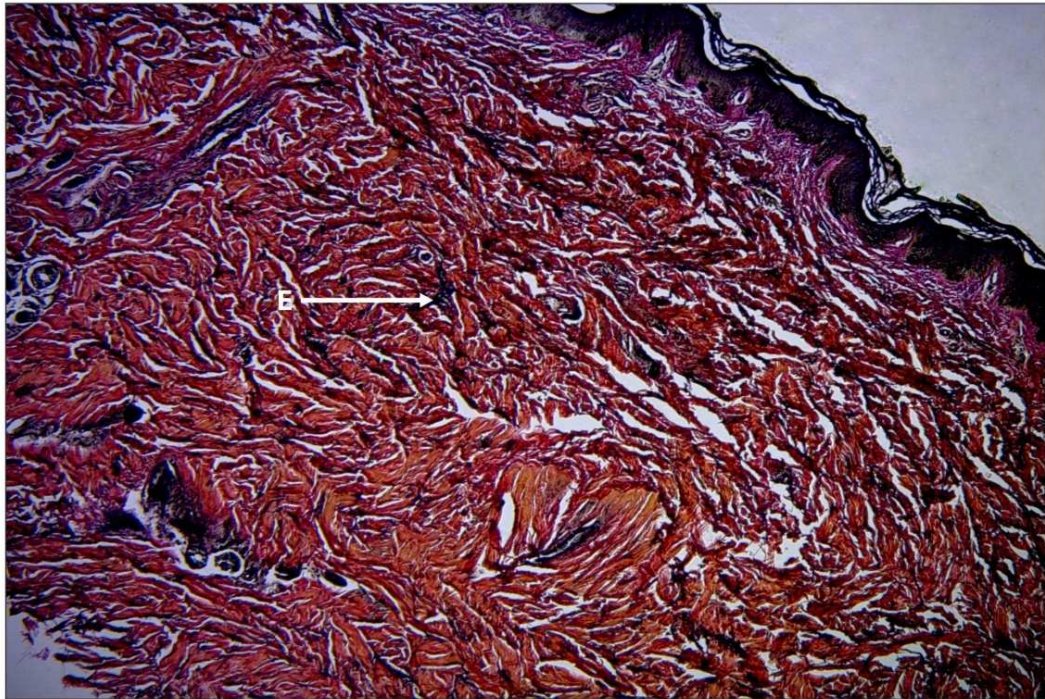


Figure 41 : Verhoeff Van Geison Stain Group B : 21 - 30 Years (10x X 10)

E : Elastic Fibers (Black) (Increased number, Thick and Elongated)

C : Collagen Fibers (Pink)(Increased number, Thick and Elongated)



Figure 42 : Verhoeff Van Geison Stain Group B : 31 - 40 Years (10x X 40)

E : Elastic Fibers (Black) (Increased number, Thick and Elongated)

C : Collagen Fibers (Pink)(Increased number, Thick and Elongated)

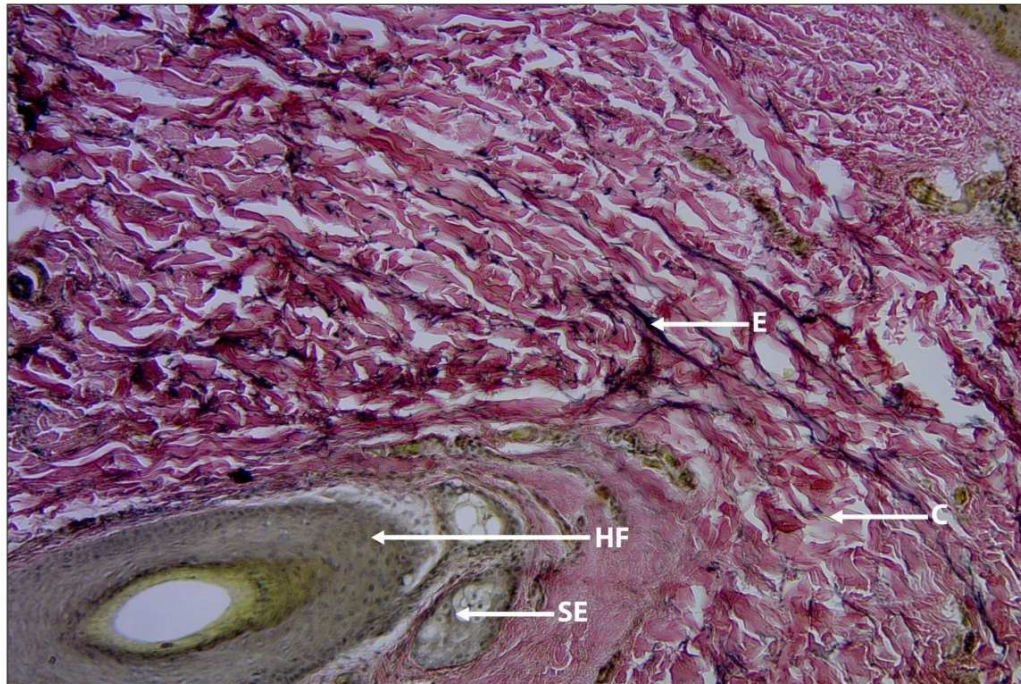


Figure 43 : Verhoeff Van Geison Stain Group B : 31 - 40 Years (10x X 10)

E : Elastic Fibers (Black) (Increased number, Thick and Elongated) HF : Hair Follicle

C : Collagen Fibers (Pink)(Increased number, Thick and Elongated) SE : Sebaceous Gland

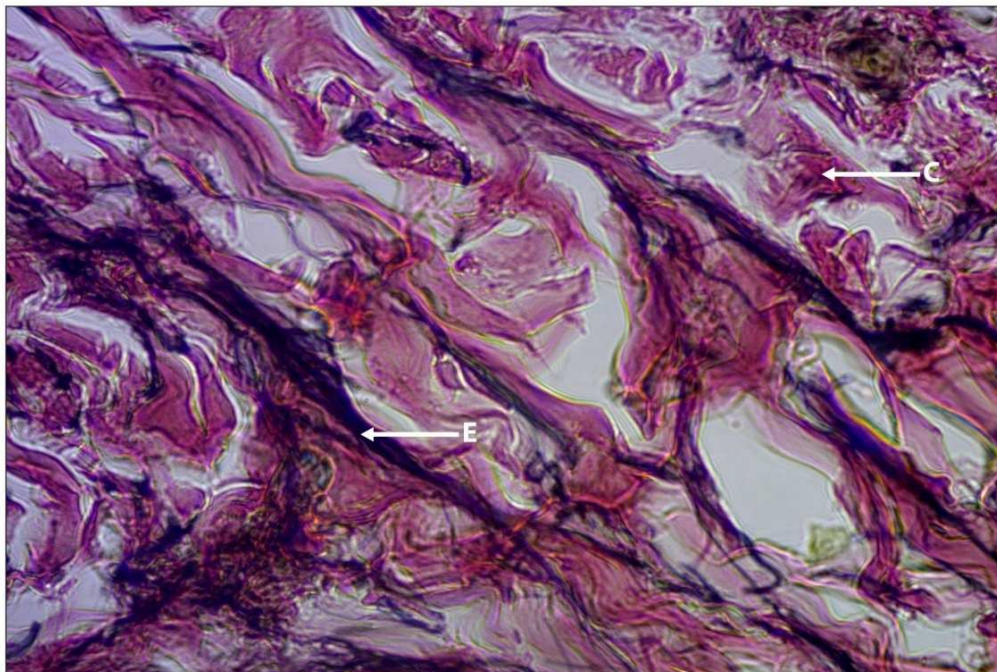


Figure 44 : Verhoeff Van Geison Stain Group B : 31 - 40 Years (10x X 40)

E : Elastic Fibers (Black) (Thick and Elongated)

C : Collagen Fibers (Pink)(Thick and Elongated)

41-50years:

The skin specimen belonging to this age group was observed to have little number of elastic fibers which were found to be fragmented.

The collagen fibers were observed to be thick, elongated and increased in quantity as found in Fig (45), (46) and Fig (47).

GROUP C:

In skin specimen of this age group, the elastic fibers were fragmented and distorted.

There was no decrease in the number of collagen fibers, but was not compactly arranged and it was found to be distributed unevenly as found in Fig (48), (49) and (50).

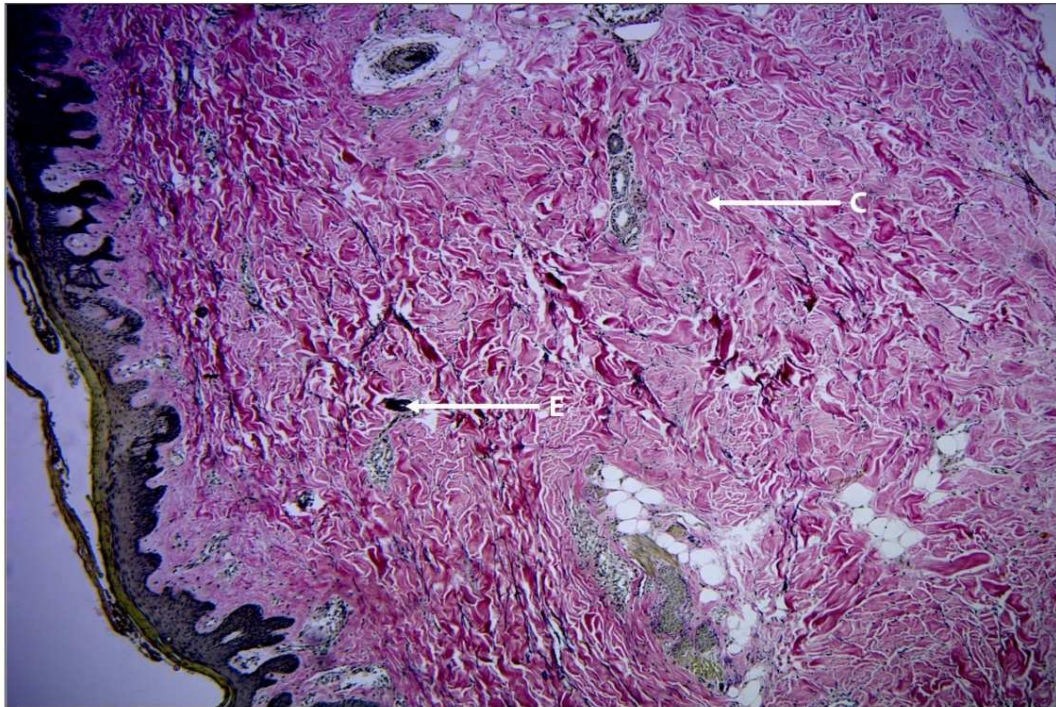


Figure 45 : Verhoeff Van Geison Stain Group B : 41 - 50 Years (10x X 10)

E : Elastic Fibers (Black) (less Number and Fragmented)

C : Collagen Fibers (Pink) (Increased, Thick and Elongated)

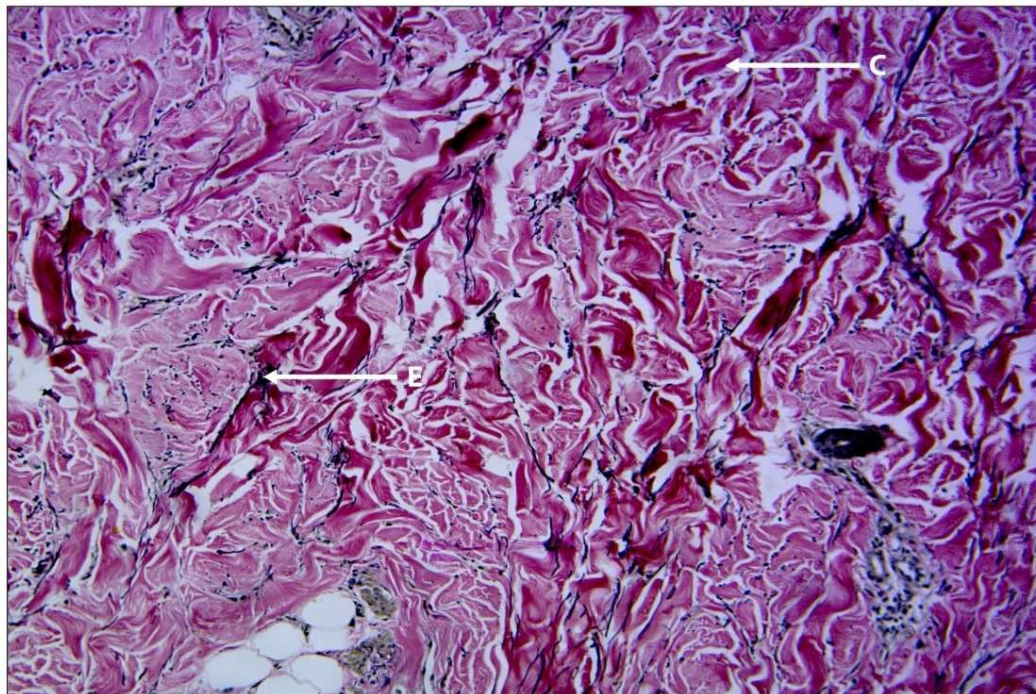


Figure 46 : Verhoeff Van Geison Stain Group B : 41 - 50 Years (10x X 40)

E : Elastic Fibers (Black) (less Number and Fragmented)

C : Collagen Fibers (Pink) (Increased, Thick and Elongated)

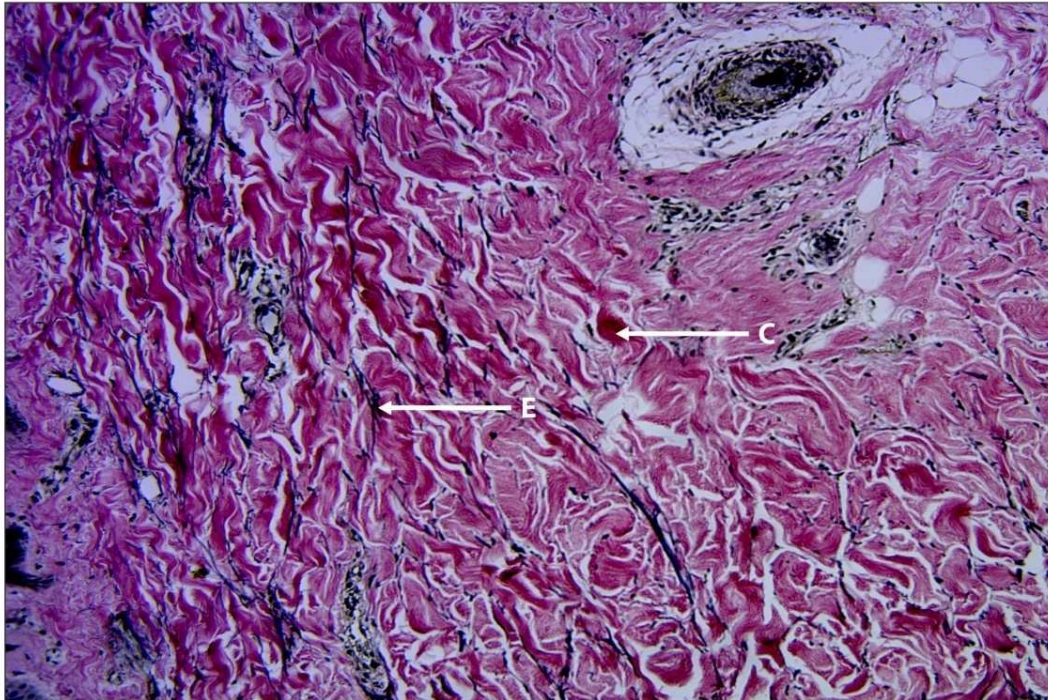


Figure 47: Verhoeff Van Geison Stain Group B : 41 - 50 Years (10x X 10)

E : Elastic Fibers (Black) (less Number and Fragmented)

C : Collagen Fibers (Pink) (Increased, Thick and Elongated)

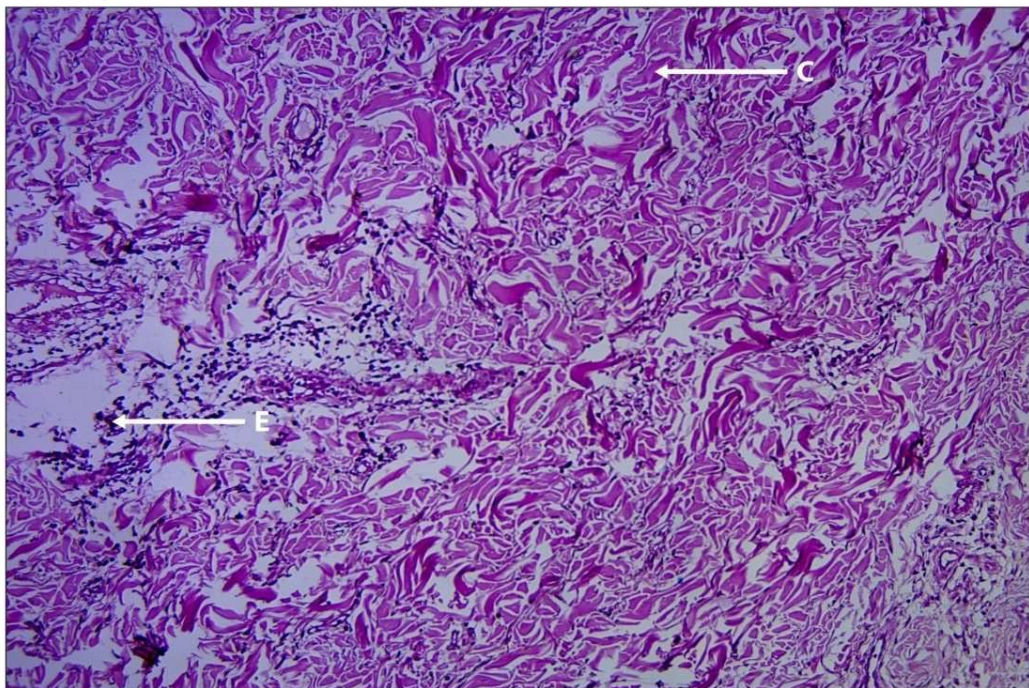


Figure 48 : Verhoeff Van Geison Stain Group C : 51 - 65 Years (10x X 10)

E : Elastic Fibers (Black) (Very less Number, Fragmented and Distorted)

C : Collagen Fibers (Pink) (Thick and Elongated)

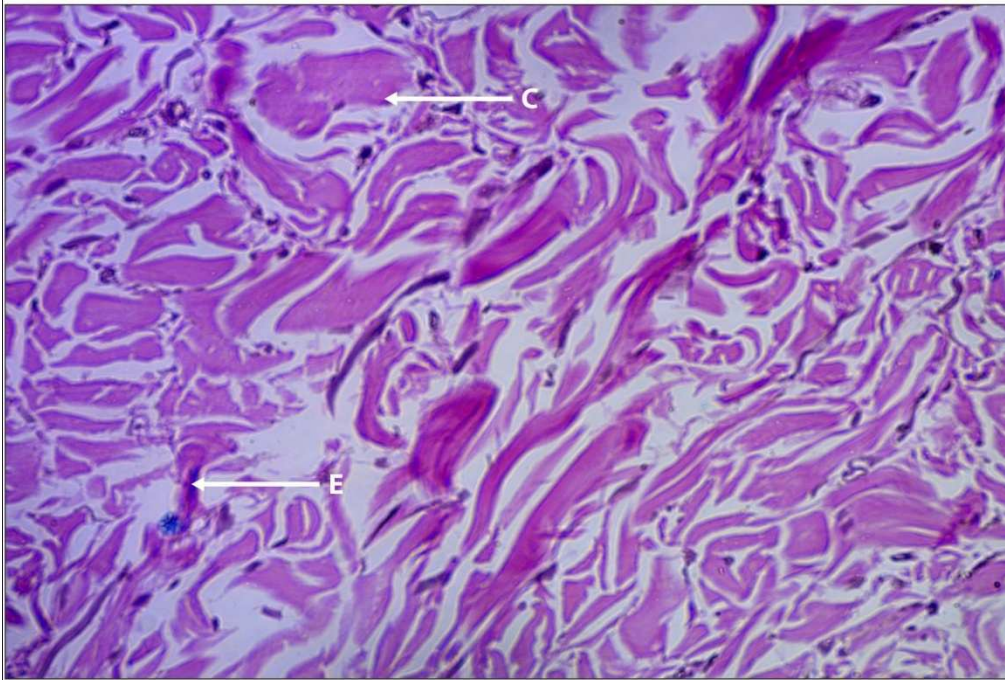


Figure 49 : Verhoeff Van Geison Stain Group C : 51 - 65 Years (10x X 40)

E : Elastic Fibers(Black) (Very less Number, Fragmented and Distorted)

C : Collagen Fibers (Pink) (Thick and Elongated)

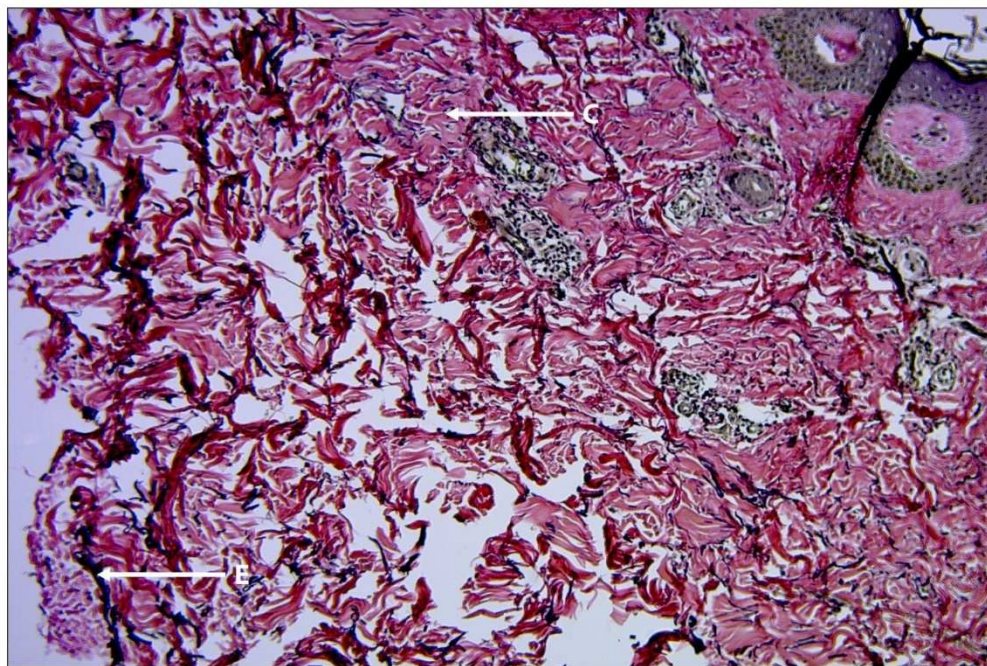


Figure 50 : Verhoeff Van Geison Stain Group C : 51 - 65 Years (10x X 10)

E : Elastic Fibers (Black) (Fragmented and Distorted)

C : Collagen Fibers (Pink) (Uneven Distribution)

GROUP D:

In this age group of more than 65 years of age, the skin specimens were observed to have decreased number of elastic fibers which were fragmented and clumped together in the dermis and the collagen fibers were also found to be fragmented and distorted in the dermis as in Fig (51).

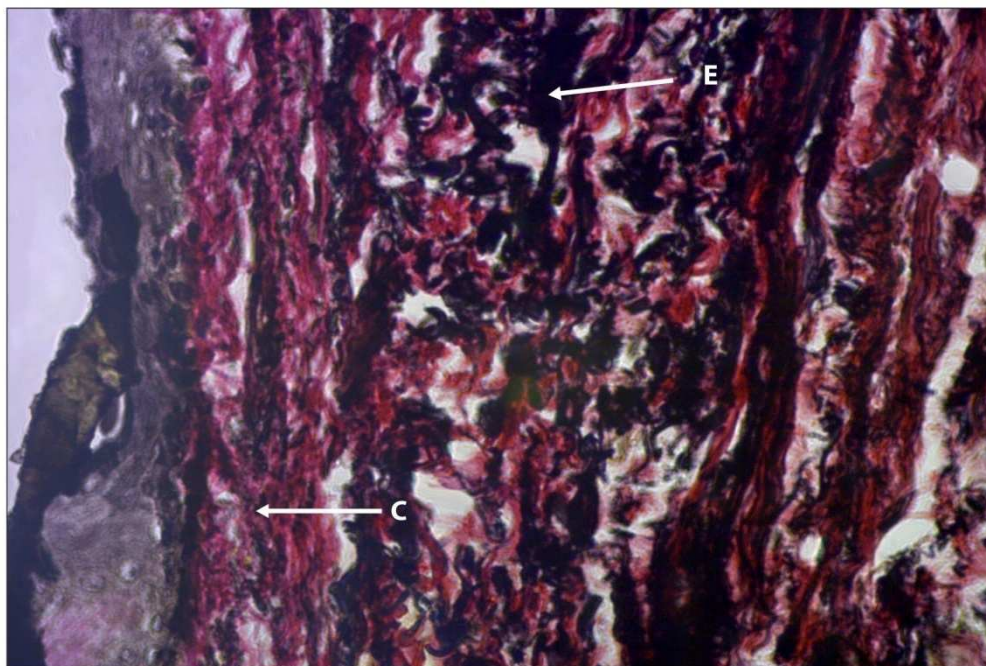


Figure 51 : Verhoeff Van Geison Stain Group D : > 65 Years (10x X 40)

E : Elastic Fibers (Black) (Fragmented and Clumped)

C : Collagen Fibers (Pink) (Fragmented and Distorted)

DISCUSSION

DISCUSSION

The various changes observed microscopically in the structure of the layers of the skin and skin appendages produces changes in the structure and functions of the skin which is mainly reflected in old age. As the average life expectancy keeps increasing, this becomes an increasing problem for the dermatologists. Most of the studies have quoted little or no difference in the structure of the epidermis and dermis in different areas of the body. But difference has been noted in the sun exposed and non-exposed areas.

Karine Cucumel (2012) has reported that, in individuals between 20-30years of age and 30-40 years of age, dermal papillae were found to be increased in number and the Dermo-Epidermal junction was highly convoluted. It was also reported that the dermal papillae started to get reduced and retracted after 40 years of age. After 60years of age the flattening of the Dermo-Epidermal junction was noted.

Coinciding with the above report in the present study it was observed that the Dermo-Epidermal junction was highly convoluted as early as 3-20 years of age and it was also observed that there was an increase in the number of Rete Pegs which was also reported in the above study. Coinciding with the above report the Rete Pegs was found to be decreased in number from 40 years of age and the Dermo-Epidermal junction was less convoluted in Group C individuals from 51-65 years of age. The Dermo-Epidermal junction was found to be flattened after 65 years of age which was similar to the above report.

Neil A Fenske (1986) has reported in his study that the epidermal thickness gets reduced with increasing age.

In contrary to the above study, the epidermal thickness was thin till 20 years of age group and it was found to be increasing in thickness from 21-50 years of age group and it was found to be very thin after 65 years of age.

Jane Sandby Moller (2003) has explained that the Stratum corneum of the epidermis is found to be thinner in sun protected areas, but becomes thick in sun exposed areas.

In accordance with this study, in the present study since both leg and foot were sun exposed areas, the thickness of the epidermis as a whole was noted and was found to be reduced with increasing age especially in Group D individuals of more than 65 years of age.

Robert M Lavker (1987) has described the microscopic features of the skin of individuals of different age groups which reveals the thinner epidermis in older individuals due to retraction of Rete Pegs. Retraction of Rete Pegs leads to flattening of the Dermo-Epidermal junction.

Similar to the above report in the present study also, the epidermis was observed to be reduced in thickness and was found to be very thin in older individuals and it was also observed that the Rete Pegs were retracted, which was leading to flattening of the Dermo-Epidermal junction.

Jeanette M Waller (2005) has reported that the thickness of the epidermis started to increase till 20 years of age, and then the thickness was remaining constant followed by thinning of the epidermis in older individuals.

This contradicts with the present study where the epidermis was found to be thin in Group A persons and the thickness started to increase after 20 years of age. The epidermis was thinned out after 50 years of age in Group C individuals with marked thinning in Group D persons of more than 65 years of age, with flattening of the Dermo-Epidermal junction.

Peter M Elias (2006) has described that the intrinsic aging changes like thinning of the epidermis and loss of Rete Pegs produces flattening of the Dermo-Epidermal junction which alters the permeability barrier of the epidermis.

In the present study also the epidermis was found to be thin with increasing age and there was loss of Rete Pegs which caused flattening of the Dermo-Epidermal junction.

A K Langton (2010) has explained that, in the skin from the abdomen, the Rete Pegs were found to be reduced and the thickness of the epidermis was also found to be reduced from 60 years of age.

These findings did not correlate with the present study as the thickness of the epidermis was found to decrease from 50 years of age. The thickness of the epidermis was reduced with increasing age.

Kakasheva-Mazhenkovaska L (2011) has reported about the structure of the skin in the scalp and has found out that the thickness of the epidermis in the scalp is maximum at the age of 22 and then it starts to decrease slowly. After 56 years the thickness gets reduced to the same value as in childhood.

In the present study the thickness of the epidermis was found to be maximum in Group B individuals of 21-50 years of age and was observed to decrease from 50 years of age and it was observed to be thinner in Group D individuals of more than 65 years of age.

W.Montagna (1990) has reported that the Dermo-Epidermal junction started to get flatten in old age. The Rete Pegs were reduced and also very blunt instead of complete disappearance.

In the present study the Dermo-Epidermal junction was found to be flattened and the Rete Pegs were observed to be blunt because of the decrease in the depth of the Rete Pegs.

Esmat Z. Gheith (1991) has reported that the Dermo-Epidermal junction was undulating in Group 1 between 20-40yrs, but in Group 2(40-60) and Group 3(60-75) the Dermo-Epidermal junction was flattened.

These findings correlated with the present study as in Group A from 3-20years, the numbers of Rete Pegs were more and the Dermo-Epidermal junction was highly convoluted. In Group B individuals between 21-50yrs of age, the Dermo-Epidermal junction was convoluted similar to Group A persons of 3-20 years of age and it was observed that there was no difference in the Dermo-Epidermal junction among the Group B individuals between 21-30, 31-40 and 41-50yrs age group. In Group C the number of Rete Pegs was found to be reduced and the Dermo-Epidermal junction was found to be less convoluted. In Group D individuals of more than 65 yrs of age, there were no Rete Pegs and the Dermo-Epidermal junction was almost flattened.

Dumas M (2008) has described that, in the papillary dermis the thin vertically oriented elastic fibers called oxytalan fibers was found to be decreased with increasing age. There was no difference in the number or density of the elastic fibers between the sun exposed and sun protected

areas of the skin, but the elastic fibers were fragmented leading to elastosis in sun exposed skin.

Similar to the study reported above in the present study, the numbers of elastic fibers were decreased with increasing age. In Group A (3-20years) and Group B (21-50years), the densities of the elastic fibers were more and the fibers were found to be thick and elongated. In Group C (51-65years) the elastic fibers were fragmented and distorted. In Group D (>65years) the elastic fibers were fragmented and clumped together in dermis.

Faten S. Cousha (1991) has reported that the collagen fiber content was reduced in the dermis. The elastic fibers showed focal loss or focal proliferation. The elastic fibers in the papillary dermis were thickened in old age.

These findings correlated with the present study as in Group D individuals of more than 65 years of age, where the elastic fibers were thickened, fragmented and clumped together in the dermis.

Esmat Z. Geith (1991) described that the dermis showed decrease in collagen fibers and increase in the elastic fibers, but the elastic fibers were fragmented and disorganized.

In the present study the elastic fibers were decreased and fragmented in the dermis in Group D individuals of more than 65 years of age.

Marinela Bonta (2013) explains about the structure of the skin, that until 50 years of age, the papillary dermis is less compact or loosely arranged. Reticular dermis is denser than papillary dermis. The collagen fibers are thin in superficial dermis and thick in reticular dermis. Age related changes started appearing in the collagen and elastic fibers after 50 years of age. The elastic fibers of the superficial dermis undergo lysis at first and then gradually the thinnest fibers disappear and the superficial dermis becomes thin in aged persons. This process of lysis extends to deep dermis. This produces spaces between the collagen fibers.

The collagen fibres are at first small and then gradually increase in size and appear thicker. At about 70 years of age the deep dermis has a more fibrous appearance. So with increasing age in deep dermis the

collagen fibers are found to be loosely packed. These findings correlated with the present study.

J Graham Smith (1965) has reported that the collagen fibers become coarse and thick with increasing age. The numbers of elastic fibers were more in the skin of the adults.

In accordance with the study reported above, in the present study, the collagen fibers were thick and coarse, but loosely packed with increasing age and the elastic fibers were more in the dermis of the adults.

Malvi (2011) explained that the collagen fibers are thick and the content of collagen fibers were reduced in old skin.

In the present study the collagen fibers were thick and the quantity of collagen fibers were not found to be reduced, but they were found to be loosely arranged and unevenly distributed.

Susan Standring (2008) describes that the natural aging process starts to get reflected from 3rd decade producing epidermal and dermal atrophy. The thickness of the Stratum corneum is not reduced in old age. So the permeability barrier is not affected. The loss of Rete Pegs producing flattening of the Dermo-Epidermal junction is reflected as decreased adhesion of epidermis to dermis. So the epidermis gets separated from the dermis even with minor injury. Photo aging mainly influences the langerhan cells and the melanocytes.

Similar to the above description the Rete Pegs were found to be reduced in depth and number and the Dermo-Epidermal junction was found to be flattened as the age increases. But the age changes were observed to be reflected from second decade of life in contrary to the above description.

Yolanda Rosi Helfrich (2008) has reported that aging produces epidermal atrophy, loss of Rete Pegs and thinner dermis, but photo aging produces marked epidermal atrophy or may also produce increased epidermal thickness. Signs of photo aging are mainly reflected in the dermis, where there is accumulation of elastin containing material just below the Dermo-Epidermal junction.

This correlated with the findings in the present study as the elastic fibers were found to be clumped in the dermis in Group D individuals of more than 65 years of age just below the Dermo-Epidermal junction.

Leslie Baumann (2007) has reported that the elastic fibers of the dermis were found to be increasing in number from fetal life. The number of elastic fibers peaks near birth and increases at the time of birth and early neonatal life. Then they start decreasing. There are two types of elastic fibers classified according to their maturity. The oxytalan fibers are the least mature fibers extending perpendicularly from the Dermo-Epidermal junction to the reticular dermis and the elaunin fibers are the more mature fibers found horizontally in the reticular dermis. The oxytalan fibers give elasticity to the young skin. These fibers were found to decrease with increasing age. Photo aging first produces hyperplasia of the elastic fibers. Later in aged skin degenerative changes occur in the elastic fibers leading to loss of skin elasticity.

In the present study the oxytalan and the elaunin fibers were not able to be differentiated. Similar to the above report the elastic fibers were found to undergo degenerative changes with increasing age like decrease in number of elastic fibres in Group C individuals of 51 years to

65 years of age and also fragmentation and clumping of the elastic fibers in Group D individuals of more than 65 years of age.

C. C. Zouboulis (2001) has reported that the secretion of sebum by the sebaceous gland falls during childhood. During puberty the secretion of sebum is increased and reaches the maximum in young adulthood. The size of the sebaceous gland is more during neonatal period, decreases few weeks after birth and is not found in childhood. The size then increases during puberty and decreases at the seventh decade of life.

In the present study the size and the number of sebaceous glands were observed not to have any significant changes with increasing age. The difference was noted only at different sites of the skin. The size of the sebaceous glands were small in the chest and abdomen. The number of sebaceous glands was found to be more in the facial region in the forehead. The sebaceous glands were found to be highly branched in the region of the cheek.

Jean Kanitakis has reported that there were 2 types of sweat glands, the eccrine and apocrine sweat glands. Eccrine sweat glands being the main sweat glands were found everywhere on the skin. They were found in the deep dermis and in the Dermo-Epidermal junction. They were made up of two rows of secretory cells, clear cells or dark cells. The secretory cells produce sweat. Dark cells were present towards the lumen of the eccrine sweat gland and contain mucopolysaccharides. Clear cells were present in the secretory coil of the eccrine sweat glands. Clear cells were identified with their foamy cytoplasm.

David E. Elder (2010) has reported the structure of the sweat glands as, clear cells having a broad base and is narrow towards the lumen whereas the dark cells are broader towards the lumen.

The sweat glands were found to have similar structure and were found to be located in the similar sites as reported in the above study. But the numbers of sweat glands were found to be less in Group A individuals of 3 years to 20 years of age and more in Group B individuals of 31 to 50

years of age and also in Group C individuals of 51 to 65 years of age and was observed to be less in number in Group D individuals of more than 65 years of age.

Kakasheva- Mazhenkovaska L (2011) has reported that the dimensions of the sweat glands were found to increase until adolescence and then started to decrease slowly.

In the present study in Group A there was less number of sweat glands. In Group B, in 21-30 years age group, the numbers of sweat glands were almost similar as in Group A. In 31-50 years age group, more number of sweat glands was found to be observed as compared to Group A persons of 3 years to 20 years of age. But the dimensions were observed to be the same in all age groups.

In Group C individuals in age group between 51-65years also there were more number of sweat glands similar to Group B individuals of 21 years to 50 years of age. But the sweat glands in Group D individuals of more than 65 years of age were found to be less in number similar to Group A individuals of 3years to 20 years of age.

CONCLUSION

CONCLUSION

Intrinsic aging predisposes the skin to various skin diseases. The various changes in the skin reflected externally act as markers for prevention and early diagnosis of systemic diseases.

The thickness of the epidermis gets reduced in old age due to altered cellular morphology. This leads to decrease in the moisture content of the Stratum corneum producing dryness or roughness of the skin, which is the common skin problem encountered in old age (1986).

The reduction in the number of dermal papillae produces flattening of the Dermo-Epidermal interface predisposing the skin of the old persons to bulla formation and various shear type of injuries. In aged persons the collagen fiber content decreases making the collagen less soluble. Its capacity to get swollen up decreases, making it more resistant to digestion by collagenase. So the collagen becomes more stable due to

changes in the number and type of cohesive bonds. So the tensile strength of the collagen fibers is exaggerated, predisposing the dermis to tear type of injuries (1986).

Following an injury, the ability to repair wounds by re-epithelialisation of the Stratum corneum is reduced in aged persons (1987).

The age changes in the dermis as reduction in the number of collagen fibers and elastic fibers is reflected externally as wrinkling, stiffness and flaccidity of the skin (2008).

Changes in the photo aged skin due to chronic sun exposure predispose the skin to various common skin disorders like xerosis, pruritis, purpurae and eczematous dermatitis (2009).

The microscopic changes in the skin in old age leads to cystic and lacunae formation. These changes make the elastic fibers more porous and the skin becomes lax (1991).

The permeability barrier of the epidermis is altered due to decrease in the number of nucleated cell layers and flattening of the Dermo-Epidermal junction. In young skin calcium level is low in Stratum basale and Stratum spinosum, but the intracellular and extracellular calcium level is high in Stratum granulosum. The normal distribution of calcium is lost in aged epidermis. This can be the reason for the altered permeability barrier in aged epidermis (2006).

The epidermis gets thinned out in aged persons. The hydration is affected producing dry, cracked, pruritic and fissured skin called xerosis. If the fissures and cracks are deep, then the dermal capillaries will be invaded producing bleeding fissures. The activity of the sweat glands and the sebaceous gland decreases and the moisture content is depleted, thereby predisposing the aged skin to xerosis (2009).

In photo aged skin, hyaluronic acid level increases. In young skin hyaluronic acid is found in the periphery of the collagen and elastic fibers where these fibers intersect. Such type of binding of the fibers with hyaluronic acid is said to disappear in old skin. Reduced water binding leads to changes in the external appearance of the skin as wrinkling, altered elasticity and reduced turbidity. The strength and resilience to the skin is provided by collagen and elastic fibers. These fibers undergo

degeneration as age advances, thereby the skin becoming more fragile and giving an aged appearance. (2012).

Aging reduces the immune function in a naturally aged skin. Following an injury after healing of the wound, scar formation occurs which is a natural process. Scar also forms due to deposition of collagen, but the collagen differs in its composition and arrangement pattern in a scar tissue. Sweat glands and hair follicles do not appear in the scar. Langer's lines reflect the orientation of collagen fibers which is the line of choice in surgical approach.

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